



**PRINCIPAL INVESTIGATOR'S
MANUAL**

Prepared by the
American College of Radiology Imaging Network
Protocol Development and Regulatory Compliance Department

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Preface

The PI Manual

This manual is designed for American College of Radiology Imaging Network (ACRIN) Principal Investigators (PIs). There are three parts: 1) the first part, for Site PIs, details the requirements for participating in an existing ACRIN trial; 2) the second part, for Trial PIs, contains information about ACRIN protocol development and implementation; and 3) the third part, the appendices, contains links to important documents online, other tools, and ACRIN policies. Site PIs are responsible for the conduct of the research specific to the study protocol at a specific institution; the Trial PI is responsible for the overall development and adherence and oversight of the entire trial. The appendices provide additional information for both Site and Trial PIs. The manual will also be useful for members of ACRIN committees working to develop protocols and protocol concepts.

This manual is intended to supplement the details found on the ACRIN web site (www.acrin.org), the ACRIN [Adverse Events Reporting Manual](#), and the ACRIN [Audit Manual](#), all of which contain more detailed information about these topics. This manual also supplements the more general [A Manual for Participants in Clinical Trials of Investigational Agents Sponsored by DCTC, NCI \(NCI Investigator's Handbook\)](#) developed by the Cancer Therapy Evaluation Program (CTEP) of the National Cancer Institute (NCI).

The American College of Radiology Imaging Network

ACRIN is an NCI Clinical Trials Cooperative Group made up of investigators from more than 100 academic and community-based medical facilities in the United States, Canada, Argentina, Germany, Korea, Israel, and the Netherlands. The goal of ACRIN is to conduct clinical research that improve the health, longevity, and quality of life for people with cancer, neuropathy, cardiopathy, and other conditions through the use of diagnostic imaging and image-guided treatment procedures.

ACRIN staff members provide clinical trial support for group investigators, such as, but not limited to administrative, data management, statistical, quality assurance, and protocol development. The data management staff (under the direction of the Biostatistics Center) and administrative staff are headquartered in the ACR Clinical Research Center in Philadelphia, Pennsylvania. The Biostatistics Center is located at Brown University in Providence, Rhode Island. ACRIN receives funding through grants from the NCI, the Pennsylvania Department of Health, and other government resources, as well as corporate and foundation support.

To contact ACRIN Headquarters, Protocol Development and Regulatory Compliance, and Administration:

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Part I: ACRIN Site Principal Investigators

1.0 SITE PI OVERVIEW: INITIAL TRIAL PARTICIPATION REQUIREMENTS

This section is a guide for ACRIN Site Principal Investigators (PIs) who take responsibility for the conduct of the trial and adherence to a specific protocol at an ACRIN-qualified institution. It describes the initial requirements for participating in an ACRIN trial. *Although a Site PI may designate research staff to assist with some of these requirements, ultimately the Site PI is responsible for ensuring adherence to federal regulations and that all initial and ongoing participation requirements are met according to the guidelines outlined in the study-specific protocol. See Appendix 4 for a Checklist of these procedures for use at your site.*

If you have questions about any of these items, please contact ACRIN Headquarters. More general information about the conduct of clinical research and PI responsibilities can be found in the *NCI Investigator's Handbook* (<http://ctep.cancer.gov/handbook>), Section 12.

1.1 Administrative Requirements

1.1.1 General Qualifying Application (GQA)

The site has submitted a [General Qualifying Application](#) (GQA) to ACRIN administration, and it has been approved by the Institutional Participants Committee (IPC).

Sites that have previously participated in ACRIN trials and have a GQA on file at ACRIN Headquarters do not need to complete another. Those sites are listed on the ACRIN web site, and can be accessed by clicking on the [ACRIN Participating Sites](#) web page. The GQA and additional information on site qualification procedures is available on the [ACRIN Application Overview](#) web page. If you have questions about the GQA, please contact ACRIN administration. Once the GQA has been approved, ACRIN is responsible for sending the site a contract.

1.1.2 ACRIN Contract

The Site PI and appropriate institutional official(s) have completed an ACRIN contract and returned it to ACRIN administration.

Please note that an institutional contract may already be in place if an institution has previously participated in an ACRIN trial. This institutional contract will be signed by the ACRIN Institution PI (who supervises all ACRIN studies at a particular site). In some cases, the same person may serve as the Site and the Institution PI. The contract must also be signed by an authorizing official (usually from a grants or contracting office) at the institution.

1.1.3 Protocol Specific Application (PSA)

The site has determined it has the required imaging hardware and software, qualified personnel, and capability to recruit the anticipated number of

participants as described in the protocol and has submitted a Protocol Specific Application (PSA) to ACRIN administration.

Each ACRIN clinical trial has its own dedicated web page on the ACRIN web site (www.acrin.org). To access the information specific to a study, including the PSA, go to the [Protocol Summary Table](#) and click on the appropriate study number. The PSA can be found under Protocol Application and Site Activation Materials. All PSAs must be approved by the ACRIN IPC.

Helpful Hint

Each ACRIN trial has its own Protocol-Specific Landing Page where important documents are posted online for easy access. The online address to reach this page is the same for every trial, with the exception of including the four-digit protocol number as follows:
www.acrin.org/####_protocol.aspx.

1.1.4 Case Reimbursement Schedule

The Trial PI has finalized the study-specific case reimbursement schedule with ACRIN Project Manager.

The case reimbursement schedule will be sent out by ACRIN administration to all sites interested in participating.

1.2 Regulatory Requirements

All study-specific regulatory documents must be submitted to the ACRIN Protocol Development and Regulatory Compliance (PDRC) department prior to receiving approval for participation in the trial, and must be kept up to date and on site for access during monitoring and auditing procedures. Optimally, all documents will be kept in a study-specific Regulatory Binder.

1.2.1 ACRIN Statement of Investigator and/or Form FDA 1572

The Site PI has completed and submitted to ACRIN administration an ACRIN Statement of Investigator and/or Form FDA 1572, along with the current CVs (signed and dated) and copies of medical licenses, as appropriate, for all personnel listed on the Statement of Investigator and/or Form FDA 1572.

Form FDA 1572 is required for all FDA-regulated research as well as any research involving an IND agent. The ACRIN Statement of Investigator is required for all ACRIN trials. These documents are available on the ACRIN web site at www.acrin.org/applicationmaterials.aspx. All CVs must be signed and dated as confirmation of their current accuracy. (A collection of document links is available in Appendix 1 of this manual.)

1.2.2 Human Research Education

All institutional staff participating in the trial has completed the NCI Protecting Human Research Participants module, or other approved education to qualify them to work with human subjects. Documentation of completion has been faxed to ACRIN administration.

The NCI module is available at <http://phrp.nihtraining.com/users/login.php>. If your institution requires an institution-specific human protections course, send the course outline and details of institution-specific requirements, such as routine renewal timelines. Send confirmation of completion of renewal to ACRIN at times conforming with local requirements.

1.2.3 OHRP Assurance

The Site PI or appropriate institution staff has faxed a copy of the institution's current OHRP-issued Federalwide Assurance (FWA) to ACRIN administration.

Whenever FWAs are renewed, send ACRIN formal notice of the FWA renewal. This information is available from your institution's Institutional Review Board (IRB). Alternatively, researchers may [search for their institution](#) through OHRP, then print out that documentation and fax it to ACRIN at 215-717-0936.

1.2.4 Informed Consent Form and IRB Approval Letter Submission

The site has modified the informed consent form template in the CTEP-approved protocol to make it site-specific and has submitted it—along with the protocol and any communications and recruitment materials—to their local IRB or Ethics Committee for approval.

Sites must modify the informed consent form template to make it specific for their institution. Sites must not delete sections from the informed consent form template, but may reword and/or expand the informed consent form per site and IRB requirements. If a local IRB requests extensive revisions to the informed consent form, please contact the ACRIN PDRC department for guidance. Please see Appendix 1 for links to appropriate resources on the ACRIN web site and Section 7.3 of the [NCI Investigator's Handbook](#) for additional details.

Please fax the documents itemized above to 215-717-0936. The site will not be able to accrue participants onto a trial until this documentation has been entered into the ACRIN database.

Helpful Hint

Regulatory documents, AE reporting details, and trial development templates are available at www.acrin.org/pdrc.aspx.

1.2.5 IND-Trial Documentation

If necessary, the site has filled out and submitted to ACRIN a confidentiality agreement and conflict of interest statement (see Appendix 2) in order to obtain the Investigator's Brochure for the IND agent.

Confidentiality agreements and conflict of interest statements may be delivered as scanned documents via email to the ACRIN Project Manager or other trial administrator (with the originals kept on file within the research record) or faxed to 215-717-0936.

1.2.6 Health Insurance Portability and Accountability Act (HIPAA)

The site has addressed issues related to the Health Insurance Portability and Accountability Act (HIPAA) per the policies of the institution and/or local IRB.

Please note that ACRIN does not monitor HIPAA compliance. Sites may incorporate the HIPAA authorization in their site-specific informed consent form or keep it separate. They may use their own authorization or they may use ACRIN's template. For more information about ACRIN's HIPAA policy, [click here](#).

1.3 Site Readiness Requirements

1.3.1 Lead Research Associate Identification

The Site PI has identified a lead RA, preferably someone with clinical research experience, who will be dedicating time to the trial.

All RAs working on ACRIN trials will have to complete the [RA Tutorial and Quiz](#) prior to working on the study. RAs will receive information and education from ACRIN about ACRIN procedures and the specific protocol details, but it is helpful to have an RA who has already participated in clinical research. It is also helpful to identify the RA early in the site readiness process so that he or she may be adequately oriented to ACRIN procedures.

1.3.2 Site Staff Work Flow and Study Site Signature and Responsibility Log

The site has identified how the trial will be conducted among institutional departments involved in recruitment and all trial procedures. The Site PI and RA have discussed and developed a formal workflow, including the involvement of other physicians, departments, and shared staff, and scheduled regular meetings. Participating clinicians and research staff have received their appropriate delegations of responsibility for the trial. Delegations have been recorded on the [Study Site Signature and Responsibility Log](#) and have included their signatures for Good Clinical Practice, trial management, and auditing purposes.

Clear communication among Site PI, RA, and other trial team members is crucial. Ultimately, the Site PI is responsible for the conduct of the trial at the institution.

Helpful Hint

The Study Site Signature and Responsibility Log is an important component of your site's preparation for activation of an ACRIN trial. It can be found online at www.acrin.org/pdrc.aspx, under "Regulatory Materials: Manuals, Policies, & Other Regulatory Binder Necessities".

1.3.3 Institutional Support/Services

The Site PI is aware of the infrastructure his/her institution provides for research support/services.

Contact your institution's research office for more information. It is important to know what resources are available to you.

1.3.4 Initial Education

The Site PI and trial team have received initial education by attending ACRIN trial-specific training sessions and meetings, participating on teleconference calls, and attending any other required informational sessions conducted by the Trial PI, ACRIN, or product manufacturers.

The Site PI, RA, and other members of the trial team will be notified of general ACRIN and study-specific training session(s) prior to activation. See Appendix 3 for information on ACRIN teleconference calls.

1.3.5 Password/Reader ID Forms

The Site PI, RA, and other members of the trial team who will be responsible for study participants and entering data on the ACRIN web site have completed the [ACRIN Username and Password and Reader ID Request Form](#) and received confirmation of their individual passwords.

This form is available through the [Application Materials](#) page of the ACRIN web site (see Appendix 1 for more helpful links) and can be found online by clicking the text in the paragraph above. Every research staff member must have his or her own password, which acts as the individual's electronic signature per 21 CFR Part 11 compliance. Passwords must not be shared with other staff members.

1.3.6 Review of Manuals

The Site PI has reviewed the ACRIN manuals, which includes this Principal Investigator's Manual, the Audit Manual, and the Adverse Events Reporting Manual.

These manuals are available on the Protocol Development and Regulatory Resources page of the ACRIN web site (www.acrin.org/pdrc.aspx).

1.3.7 Study-Specific Requirements

The Site PI has ensured that any other study-specific requirements are met (such as submission of test cases, scanner qualification, etc.).

These requirements are protocol-specific and will be detailed in the PSA, Protocol Activation Checklist, and in the individual protocol. On the ACRIN web site, each protocol has a web page with study-specific details and documents. (Go to the [Protocol Summary Table](#) to find the number of your trial, and then click on the Protocol Activation and Site Applications Materials link in the left navigation panel of the study-specific page.) Content is routinely posted online after the approval of the initial protocol draft or immediately prior to trial activation.

1.3.8 Recruitment Plans

The Site PI and RA have developed patient recruitment plans, including complying with local IRB requirements and/or working with the institution's public relations department, if feasible, to promote awareness of the study within the institution and community.

Initial recruitment plans should be in place before accrual begins. Sites can work with ACRIN's Communications department to develop plans and recruitment materials (brochures, informed consent flipcharts, etc). Some institutions also offer valuable public relations resources for clinical research.

1.4 Imaging Requirements

1.4.1 Imaging Processes

Imaging requirements vary by protocol and are delineated in detail in the protocol and on the protocol-specific web page online. (Go to the [Protocol Summary Table](#) and find the number of your trial, and then click on the Imaging Materials link in the left navigation panel of the study-specific page.) It is important to be aware of the imaging requirements and your institution's IT processes and policies.

1.4.1.1 Imaging Team Responsibilities

The Site PI is responsible for the overall conduct of the imaging for the trial, and may designate imaging components to appropriate research staff and imaging specialists. Each member of the site imaging team should have responsibilities defined in the [Study Site Signature and Responsibility Log](#) prior to initiation of the trial.

Helpful Hint

The Study Site Signature and Responsibility Log is an important component of your site's preparation for activation and conduct of an ACRIN trial. It can be found online at www.acrin.org/pdrc.aspx, under "Regulatory Materials: Manuals, Policies, & Other Regulatory Binder Necessities".

1.4.1.2 Dedicating Scanner Time for Research

The Site PI is responsible for establishing time for research on an ACRIN-qualified scanner and is responsible for the overall adherence of the site to protocol-specific parameters.

1.4.1.3 Image Submission

The Site PI implements processes for imaging completeness and timely submission of images to ACRIN for the protocol and has coordinated those processes with the institutional IT department as necessary.

Helpful Hint

Each new ACRIN trial has its own Protocol-Specific Imaging Materials page online where important imaging parameters and related documents are posted for easy access. The online address to reach this page is the same for every trial, with the exception of including the four-digit protocol number as follows:
www.acrin.org/####_imagingmaterials.aspx.

1.4.2 ACRIN Personnel Visit

If applicable, imaging personnel from ACRIN may conduct a site visit to configure equipment for image transfer and conduct on-site training.

This requirement is protocol-specific. You will be contacted by ACRIN if this is necessary.

1.4.3 Quality Assurance and Quality Control Processes

The Site PI is aware of the ACRIN [quality assurance](#) (QA) processes for the entire trial and 100% quality control (QC) review of images. Once aware of QA and QC measures for the trial, site will be able to comply with them.

QA and QC processes are specific to each protocol and will be found in the protocol itself or in a separate study-specific manual.

2.0 SITE PI OVERVIEW: ONGOING TRIAL PARTICIPATION REQUIREMENTS

This section describes the ongoing requirements for sites participating in an ACRIN trial. For additional information, see Section 12 of the [NCI Investigator's Handbook](#), "The Organization of a Clinical Trial." If you have questions about any of these items, please contact ACRIN Headquarters. **See Appendix 4 for a Checklist of these procedures for use at your site.**

2.1 ACRIN Reports and Reminders

The Site PI or designated research staff responds promptly to all reports received from ACRIN Headquarters (forms due reports, data queries, IRB approval expiration notices, etc.).

ACRIN uses these notices to convey important information to site staff. If the Site PI designates his/her staff to respond, the PI should make sure that the designee responds promptly and follows the issue until it is resolved. **It is important to inform ACRIN of any changes in research staff.**

2.2 Adherence to Protocol and Monitoring/Audit Preparation

The Site PI ensures that his/her own site adheres to protocol procedures; is prepared for site monitoring and site audit; and follows up promptly with any discrepancies, clarifications, or recommendations from the trial team.

Detailed information about ACRIN monitoring and audit requirements can be found in the ACRIN [Audit Manual](#) and either in the applicable section of the protocol or in a separate set of study-specific guidelines. General information is available in Section 16, "Monitoring and Quality Assurance," of the [NCI Investigator's Handbook](#).

2.3 Adverse Events Reporting

The Site PI is responsible for the reporting of all study-related adverse events, especially serious adverse events, in compliance with ACRIN and NCI-Cancer Imaging Program, Food and Drug Administration, or other regulatory requirements.

Detailed information about ACRIN adverse events reporting requirements can be found in the ACRIN [Adverse Events Reporting Manual](#) and in the adverse events section of the protocol.

2.4 Staff Oversight

The Site PI meets with the RA(s) and any other research staff on a regular basis to ensure that the clinical trial is being conducted in compliance with the protocol, images of adequate quality are being produced, and all forms and data clarifications to ACRIN queries are being submitted to ACRIN in a timely manner.

Regular meetings facilitate clear communication between the research staff and Site PI. Ultimately, the Site PI is responsible for the conduct of the trial at the institution.

2.5 ACRIN Statement of Investigator and/or FDA Form 1572

The Site PI is ultimately responsible for ensuring all regulatory documentation specific to IND trials (e.g., [Form FDA 1572, Study Site Signature and Responsibility Log](#)) is updated, current, and submitted to ACRIN as necessary.

Any changes to Section 6 (related to subinvestigators) of the Form FDA 1572 and/or to Section 2 of the ACRIN Statement of Investigators will need to be submitted to ACRIN. (Each updated document will need to be signed and dated by the Site PI prior to submission to ACRIN.) Personnel changes will need to be documented on the [Study Site Signature and Responsibility Log](#).

2.6 For IND Trials: Coordinating Agent Orders, Storage, and Administration

The Site PI ensures investigational agents are available, stored, and administered per DCTD (see Sections 9, 14, and 15 of the [NCI Investigator's Handbook](#)) and protocol-specific guidelines.

The Site PI and designated research staff coordinate the order and delivery of agent through the Pharmaceutical Management Branch (PMB) or protocol-specified supplier and adhere to CTEP policies for investigational agent use, storage, and distribution.

2.7 Local IRB Correspondence

The Site PI ensures that all protocol amendments, requests for annual study approval/renewal, and participant recruitment materials are submitted to the local IRB, and all approval documentation is sent to ACRIN PDRC in a timely manner. Reports from quarterly trial review by the Data and Safety Monitoring Board/Committee (DSMB or DSMC) are posted online after the meeting for download and submission to the local IRB per institutional policy.

Amendments will be circulated to all Site PIs and RAs via e-mail. The e-mail will specify whether expedited or full-board review is required; if not specified, sites are to defer to their local IRB procedures. All studies must be reviewed annually by the local IRB, and review documentation must be faxed to the ACRIN PDRC department at 215-717-0936. If IRB approval is listed as “expired” in the ACRIN database, the site will not be allowed to accrue until IRB approval is confirmed. DSMB/DSMC memos are available via the [Protocol Summary Table](#)—after clicking on the number of your trial, go to the Site Memos page via the link in the left navigation panel of the study-specific page.

2.8 Teleconference Call Participation

The Site PI or a PI-designated representative is present on all required teleconference calls.

Important information about the conduct of the study is conveyed on the teleconference calls (see Appendix 3). Calls also offer opportunities for all Site PIs and RAs to ask questions and share challenges they are facing with the trial.

2.9 ACRIN Meeting Attendance

The Site PI(s) and RA(s) attend ACRIN meetings as requested.

The ACRIN Fall Meeting is open to all ACRIN investigators, and all Site PIs and RAs are encouraged to attend protocol-specific and general sessions. The ACRIN Spring Meeting is by invitation only; those Site PIs and RAs who are invited will be notified in advance by ACRIN Headquarters.

2.10 Participant Accrual Monitoring

The Site PI and RA(s) monitor participant accrual progress and report any specific recruitment barriers to the Trial PI and the Protocol Team.

Sites are encouraged to work with the ACRIN Communications department, the protocol-specific recruitment specialist if applicable, and the Trial PI if they have any questions or concerns.

Helpful Hint

Sites may be asked to keep a Screening Log on site to aid in identifying reasons patients opt not to join the trial; this tool can be instrumental in quickly and confidently identifying recruitment barriers.

2.11 Recruitment Plans

The Site PI and RA(s) adjust participant recruitment plans and modify procedures, as determined by ACRIN, local IRBs, or institutional PR resources, as necessary to improve distribution of communication materials, educational sessions at departmental meetings, regular contact with referring physicians, etc.

Recruitment issues will be discussed on teleconference calls (see Appendix 3) and at ACRIN meetings. When possible, ACRIN will work with sites to create additional communication materials.

2.12 Requesting Waivers to Eligibility and Other Protocol Requirements

The Site PI requests approval via ACRIN Data Management or the ACRIN Director of PDRC for a waiver to eligibility criteria or other protocol requirements. The Site PI must await final approval from the ACRIN Network Chair prior to proceeding with registration or the procedure.

Once the request is made to ACRIN Data Management or the ACRIN Director of PDRC, the Trial PI will be contacted by ACRIN for an initial decision whether to reject the waiver request. If the Trial PI rejects the request, the Site PI will be informed. If the Trial PI approves of the waiver, he/she informs the ACRIN Director of PDRC, who directs the request to the ACRIN Network Chair for potential final approval. The Site PI will be informed of the final decision and how to proceed.

PART II: TRIAL PRINCIPAL INVESTIGATORS

3.0 ACRIN CONCEPT AND PROTOCOL DEVELOPMENT AND SUBMISSION PROCESS

The principal business of ACRIN is the conduct of rigorous, multi-institutional, multidisciplinary clinical research. Although ACRIN provides the financial support necessary to conduct its own research, ACRIN is not a funding agency. Rather, it provides a centralized infrastructure for the conduct of clinical trials and includes among its functions: protocol design; biostatistic services; data and image transmission, storage/archiving, and management; the development and maintenance of standards; quality assurance; and data analysis. Investigators recruited by ACRIN to conduct its research employ this infrastructure to support trial development, implementation, analysis, and results dissemination. ACRIN has designed processes and procedures to accelerate the development of competitive protocol ideas into clinical implementation. All interested parties—including radiologists, commercial vendors, insurers, and organizations—may submit protocol ideas to ACRIN for consideration of ACRIN implementation.

The process is described below and illustrated in the process maps that follow. LOI/Concept and protocol development must adhere to Operational Efficiency Working Group (OEWG) timelines.

For an overview of the OEWG timelines, see <http://ctep.cancer.gov/SpotlightOn/OEWG.htm>.

3.1 Research Idea Submissions

An idea for a clinical trial is proffered informally either within a Scientific Committee, by an individual or entity from outside of ACRIN, or by the ACRIN Advisory Panel or Steering Committee.

Any individual or entity may suggest an idea for a clinical trial and have it be considered by an [ACRIN Scientific Committee](#) dedicated to specific disease sites (e.g., cardiovascular), disease types (e.g., gynecologic cancers), or specialties (e.g., experimental imaging).

3.2 Consideration of Idea by Scientific Committee

The idea is considered by the appropriate Scientific Committee, which decides either to develop the idea into a preliminary concept or to reject it.

Decisions are based on whether the idea is important, consonant with the Committee's strategy, and in prospect, likely to result in a successful trial.

3.3 Scientific Committee Appoints Initial Protocol Concept Team Members

The Scientific Committee appoints key individuals to develop the idea into a preliminary concept.

A preliminary concept includes the key hypotheses to be addressed, basic projections of what technologies and methods will be employed, the basic trial design, and a rough estimation of sample size. The [ACRIN Preliminary Concept Development](#)

[Form](#) should be used (see Appendix 1 for links to concept and protocol development documents online).

3.4 Preliminary Concept Presented to ACRIN Steering Committee

The individual appointed by the Scientific Committee to be responsible for concept development presents the preliminary concept to the ACRIN Steering Committee for preliminary approval.

The ACRIN Steering Committee decides whether to move forward with further development of the concept based on: whether the concept is consonant with ACRIN's strategy, its importance in competition with other possible trials that might present themselves, and the availability of resources to support trial development and implementation. If the research idea is to move forward, the Scientific Committee appoints the Trial PI.

Depending on the funding source and dynamics of the concept, the trial will move forward to concept development for submission to the Cancer Therapy Evaluation Program (CTEP) or may proceed to full protocol development for CTEP or other regulatory agency review and approval. (See Section 4 of the [NCI Investigator's Handbook](#) for details of Phase 1 Trials development for CTEP-funded research. See Section 5 for details of Phase 2 Trials development; Section 5.6 describes the Letter of Intent [LOI] process and guidelines for submitting LOIs, concepts, or full protocols for CTEP consideration. See Section 6 for details of Phase 3 Trials development.)

About LOIs & Concepts

A note about Letter of Intent (LOI) versus Concept submission of initial trial ideas to CTEP:

- LOIs are an investigator's declaration of interest in conducting a Phase 1 or 2 trial with an investigational agent supplied by the DCTD for study in a particular disease;
- LOIs are developed for submission of trial ideas conceived for 100 or fewer participants;
- Concepts are developed for submission of trial ideas conceived for more than 100 participants;
- In some situations, after LOI submission, CTEP may request full Concept submission prior to protocol development.

3.5 LOI/Concept Development for Regulatory Scientific Review (CTEP or Other)

Concepts approved by the ACRIN Steering Committee undergo further development and submission as more robust concepts to CTEP (either as a formal LOI or concept) and/or other appropriate regulatory agencies.

The Scientific Committee will add members to the Protocol Concept Team. The trial team at this stage will comprise the Trial PI, co-investigators, lead statistician, medical writer, project manager, and patient advocate, at minimum. The Protocol Concept Team adds detail to the concept document (LOI or concept format, using

either ACRIN's form for Steering Committee submission followed by CTEP submission form completion) as they prepare it for submission by the medical writer or protocol associate to CTEP or another appropriate regulatory agency. The concept document is forwarded to the Outcomes and Economics Committee to evaluate the potential Outcomes and Economics aims in the trial.

Concepts submitted to CTEP must use the CTEP [Protocol Concept Submission Template](#), which should correspond with the most current version of the CTEP [LOI or Concept Submission Forms](#). Trial PIs will have to be available for scheduled CTEP-driven calls to discuss the LOI/Concept per OEWG review structure. ACRIN will inform the Trial PI of the appointed date and time as soon as possible.

3.6 ACRIN Steering Committee Makes Final Decision to Pursue Trial Protocol

Following the recommendation by CTEP (for example), the ACRIN Steering Committee makes a final determination of whether it will pursue protocol development and eventually open the trial.

The principal consideration for final approval to move forward with protocol development is whether ACRIN has the financial, software, hardware, infrastructure, IT, operational, and human resources required.

3.7 A Plan and Timeline Are Developed

The Protocol Concept Team, Biostatistic and Data Management Center, and ACRIN Headquarters collaboratively develop a timeline for future activities to meet OEWG time lines for concept through trial activation, and assign roles and responsibilities to members of the expanded Protocol Team.

3.8 Protocol Development

(To Be Submitted Within 60 Days [~8 Weeks] of CTEP LOI/Concept Approval)

The Protocol Team develops the protocol, including revisions requested or recommendations made by CTEP (or other regulatory agency) that may or may not require an accompanying responses document, and submits the protocol with [Protocol Submission Worksheet](#) for CTEP approval. The Protocol Team must be mindful of OEWG timelines according to trial phase, time outs as defined by the OEWG, and review committee schedules.

Protocol Teams should include: the Trial PI; additional imaging and non-imaging specialists who are experts in the disease site and technologies represented in the trial, including those willing to serve as co-chairs for the trial's duration; statisticians and other methodologists; ACRIN Headquarters personnel (e.g., project manager, protocol associate/medical writer, regulatory, data management, QA Committee liaison, and monitoring and audit designees); a patient advocate; and such other experts as are necessary to develop a rigorous protocol.

The Protocol Team, led by the Trial PI, begins to develop the protocol. CTEP allows 60 days from LOI/concept approval until the submission deadline for the initial protocol draft. The timeline generally breaks down into the following steps: The

protocol associate will incorporate concept components into ACRIN's protocol template appropriate for the trial and will send a first draft of the protocol electronically to the Trial PI within approximately 2 weeks of concept approval. The Trial PI may review and introduce additional background and other inclusions, or may request that the first draft go to the entire Protocol Team. The Protocol Team members then have 2 weeks to deliver text for their appropriate sections to the protocol associate to include in the master draft of the protocol, especially the study aims, statistical section, and procedures descriptions that will drive the rest of the protocol. The following 2 weeks are dedicated to full Protocol Team review of the completed draft. The final 2 weeks prior to the final submission deadline mandated by CTEP should focus on finalizing language, correcting discrepancies, and trouble shooting the outlined research.

Teleconference calls will be held routinely for protocol development (see Appendix 3). The protocol associate will maintain the master protocol document and will distribute the most up-to-date version of the protocol prior to each teleconference. A full protocol draft in almost-final version is sent simultaneously to the Protocol Team for final review prior to submission to CTEP. The Trial PI gives final approval to the protocol associate for submission.

At that point, the protocol associate makes any final edits and submits the protocol to CTEP (or other regulatory agency, e.g., the Food and Drug Administration, Radioactive Drug Research Committee, ACR Institutional Review Board [IRB]) for review. Trial PIs will have to be available for scheduled CTEP-driven calls to discuss the protocol per OEWG review structure. ACRIN will inform the Trial PI of the appointed date and time as soon as possible. The protocol is then either approved outright, approved with recommendations/comments, or returned with comments that need to be addressed within 2 to 4 weeks with a resubmission of the protocol with revisions introduced. If comments are returned, the Protocol Team revises the protocol and resubmits it with a formal response to comments until CTEP approves the protocol. The protocol must also be approved by the ACR IRB; that submission may be simultaneous with CTEP submission. Protocol-specific forms must be finalized during the approval and comment/response interaction, if not earlier.

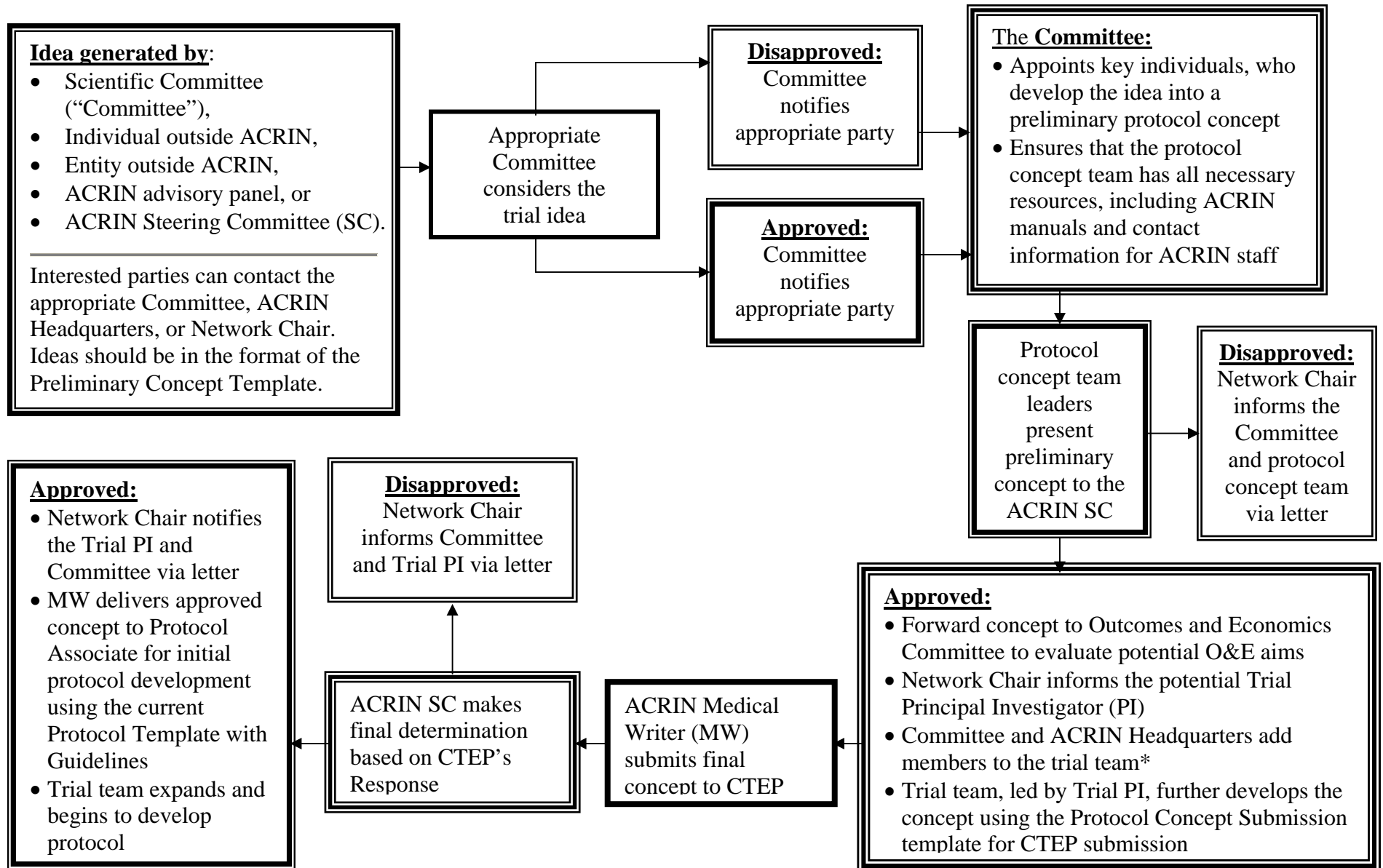
3.9 Protocol Approval, Local IRB Submissions, and Trial Activation

CTEP approves the protocol. The trial is activated depending on site readiness, funding confines, and/or completion of logistical elements, such as trial-specific manuals, activation amendments, and forms development.

Once the protocol is CTEP and ACR IRB approved, participating sites must submit the protocol to their institutional IRBs for approval, including a site-specific informed consent form. ACRIN may activate the trial prior to local site IRB approval. The Protocol Team determines a target activation date for the trial, depending on estimated local IRB approvals, site and imaging/scanner qualification, forms completion for registration of participants, site recruitment, training needs, development of manuals for imaging, pathology, biomarker processes, etc. The site will receive any necessary hardware and software for the trial or for submission of

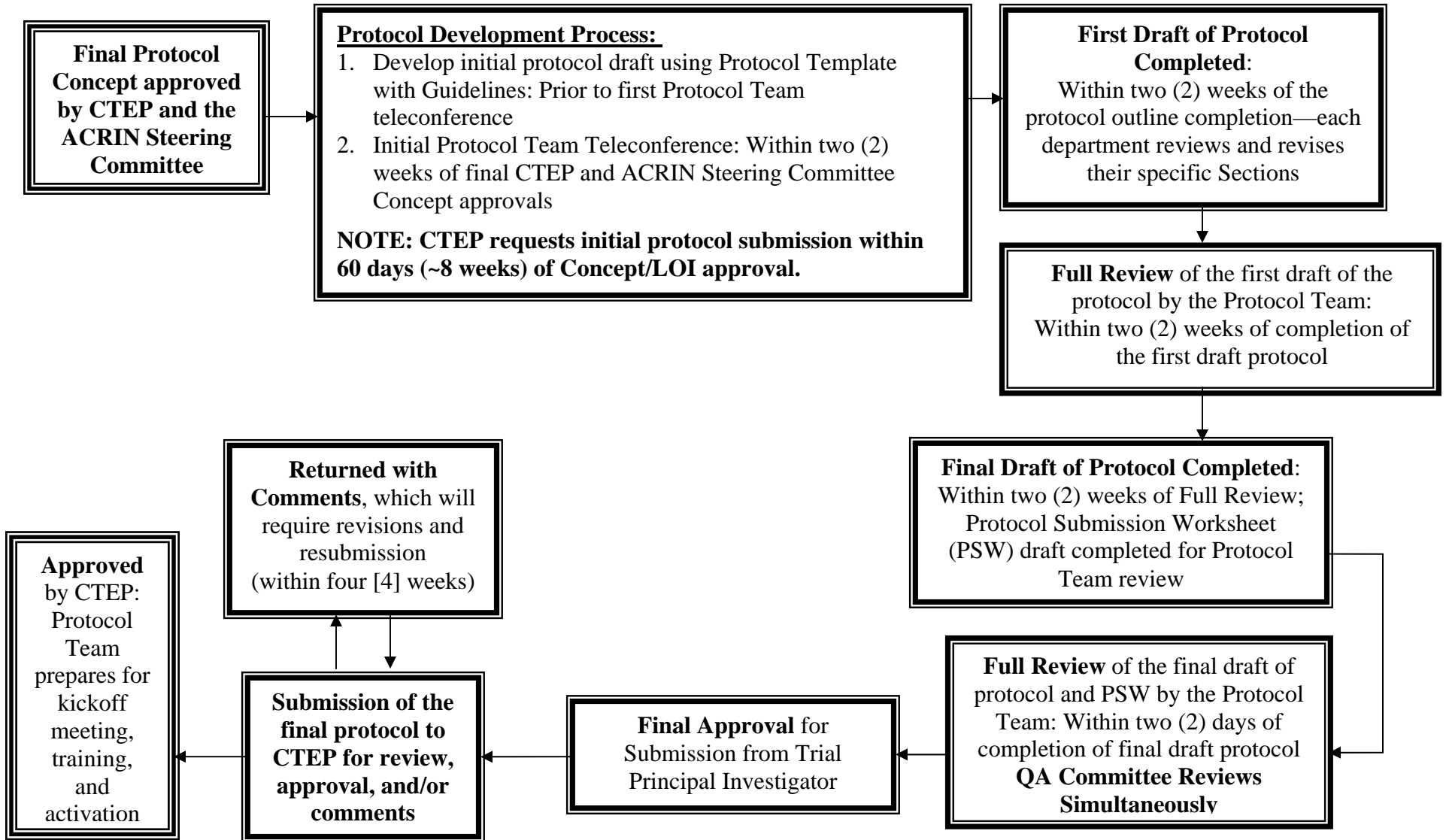
imaging materials to ACRIN for imaging/scanner qualification. Contractual agreements between institutions and ACRIN, or addenda to existing contracts, also are finalized during this period. At that point, the Protocol Team, led by the Trial PI, begins planning protocol-specific training for Site PI, RA, and other research staff education. After the trial is activated and sites have completed all regulatory requirements and qualification procedures, including local IRB approval, sites may begin accruing.

FIGURE 1. ACRIN CONCEPT DEVELOPMENT AND SUBMISSION PROCESS



The Protocol Development and Regulatory Compliance Department will be available for assistance at all phases of concept and protocol development
 *"Trial Team" comprises Principal Investigator, Co-Investigators, Lead Statistician, Medical Writer, Project Manager, and Patient Advocate, at minimum.

FIGURE 2. ACRIN PROTOCOL DEVELOPMENT PROCESS AND TIMELINE



4.0 TRIAL PRINCIPAL INVESTIGATOR RESPONSIBILITIES

Active participation of the ACRIN Trial PI during all stages of protocol development and activation is crucial to the success of the trial. The following list provides an outline of Trial PI responsibilities at each stage of the trial. More general information about PI responsibilities can be found in the [*A Manual for Participants in Clinical Trials of Investigational Agents Sponsored by DCTC, NCI \(NCI Investigator's Handbook\)*](#) developed by NCI/CTEP.

4.1 During Protocol Development:

- Leads and assists the protocol associate in the development of the protocol, including the informed consent form template and appendices;
- Considers the importance of eligibility criteria in relation to the science of the trial, factors that might limit recruitment, and Human Subjects Protections and risks associated with the study-related procedures (e.g., use of gadolinium or other contrast agents, radiation exposure for multiple imaging studies);
- Considers expectations of participants in relation to disease burden;
- Works with protocol associate to develop step-by-step procedures for trial conduct, keeping in mind that time points should likely include a range of dates to allow for scheduling, disease complications, treatment toxicity, and other factors that might cause protocol deviations from a compressed time frame;
- Interacts with the outcomes experts, statisticians, and other methodologists as required for protocol development and outcomes-analysis processes;
- Assists in coordinating pilot submissions of data forms prior to study activation;
- Assists ACRIN imaging personnel in establishing and implementing quality assurance (QA) processes for images;
- Leads imaging team to develop imaging management plan for the trial, including determination of modality, use of agents, procedures and technical parameters (especially for experimental imaging techniques), quality control, etc.
- Interacts with key experts to establish standardization of technical parameters for protocol images;
- Assists in planning the operational aspects of the protocol and its related secondary studies;
 - Assists in developing, detailing, and implementing reader studies;
 - Assists ACRIN Headquarters staff in developing a budget, selecting sites, and developing and monitoring the protocol development timeline;
 - Assists in development of the Protocol-Specific Application;
- Supports ACRIN Headquarters staff in qualifying sites that wish to participate and helps ensure their ability to submit images according to the requirements of the protocol;
- Finalizes monitoring and auditing plans with ACRIN regulatory compliance team. (Also, see Section 7 of the [*NCI Investigator's Handbook*](#), Section 6 (Special Considerations) of the PI Manual and Appendix 1, which provides links to documents online.)

4.2 Throughout Development, Study Activation, and Accrual:

- In collaboration with personnel at ACRIN Headquarters, develops the agenda and leads the discussions on protocol-specific teleconference calls (see Appendix 2);
- Provides reports and updates on the protocol to the ACRIN Steering Committee, as requested;
- Attends all ACRIN Annual Meetings:
 - Presents the status of the trial at Annual Meetings when requested;
 - Leads meeting sessions devoted to protocol development, implementation, and ongoing needs for the success of the trial;
 - Dictates minutes from meetings to include action items and highlights;
- Plans and leads training session(s) to prepare Site PIs, RAs, and other research staff for the activation of the study;
- Continues to educate sites as necessary during the course of the trial to help ensure appropriate conduct of procedures and adherence to regulations (the Trial PI is ultimately responsible for the overall conduct of the trial);
- Monitors trial accrual (site level):
 - Follows up with PIs at sites not meeting accrual goals to assess accrual barriers;
 - If necessary, develops and monitors a remedial plan to improve accrual;
- Monitors trial accrual (trial level):
 - Notifies disease site and/or modality Scientific Committee chairs and ACRIN Steering Committee via written communication should trial accrual fall under 75% of the expected accrual rate at any point after the trial reaches one quarter of the expected accrual time;
 - Identifies accrual barriers to include in the written communication to committees;
 - Develops and presents plans for addressing the barriers;
- Participates in meetings of the DSMC (or DSMB for ACRIN PA trials), and responds to DSMC and DSMB questions and concerns.

4.3 While Study Is Active:

- In collaboration with the study statistician, leads monitoring study progress, including overseeing accrual, data collection, and data monitoring;
- Answers protocol-specific eligibility and procedural questions;
- Fields waiver requests from Site PIs (e.g., to override eligibility criteria or study procedures). When a Site PI requests a waiver, the ACRIN Director of PDRC will contact the Trial PI to ask him/her to consider the request. If the Trial PI disagrees with request, he/she may reject the request outright, and the ACRIN Director of PDRC will inform the Site PI; if the Trial PI agrees with the request, the ACRIN Director of PDRC will contact the ACRIN Network Chair to obtain final approval or disapproval of the request, and subsequently inform the Trial PI of the final decision and deliver response back to the Site PI;
- Directs protocol revisions (amendments or administrative updates) with protocol associate that might be necessary to clarify or correct procedural outlines and descriptions or that might enhance accrual;
- Assists in establishing target accrual goals for participating sites;

- Interacts with participating Site PIs and appropriate ACRIN staff to promote patient recruitment, including development of specific recruitment strategies;
- Continues planning reader studies, including additional data forms development.

4.4 After Study Closes to Accrual:

- Continues to work with the Protocol Team, other investigators, and participating sites to complete participant follow up and ensure adequate data collection;
- Works with Protocol Team on implementing sub-analyses and the initiation of reader studies.

4.5 After Study Is Completed:

- Works with the Biostatistics and Data Management Center (BDMC) to clean up the data;
- Organizes and leads the work on preparation of manuscripts for publication.

5.0 MEMBERS AND RESPONSIBILITIES OF THE PROTOCOL TEAM

In addition to the Trial PI, the following people comprise the Protocol Team: protocol statistician, master's level biostatistician, project manager, coordinating and staff data managers, protocol associate (or medical writer), monitor(s), auditor(s), imaging specialist(s), patient advocate, recruitment specialist (if applicable), QA Committee liaison, intergroup liaison (if applicable), and additional experts as appropriate. Depending on the size and scope of a protocol, more than one protocol statistician and master's level biostatistician may participate in the Protocol Team. All administrative support for the development and implementation of protocols (including support for teleconference calls and preparation of documents) is provided by ACRIN Headquarters.

See below for descriptions of the duties of each member of the Protocol Team.

5.1 Protocol Statistician

During protocol development, the protocol statistician works with the Trial PI and other investigators to refine study aims; determine study design; develop language for primary, secondary, and exploratory endpoint(s); and establish operating procedures for the study, including QA. The protocol statistician also determines adequate study size and plans interim, futility, and final analyses.

When the protocol is active, the protocol statistician oversees BDMC monitoring of patient accrual and data collection and quality, coordinates data analyses and preparation of appropriate reports, collaborates with other members of the Protocol Team in the preparation of abstracts and manuscripts, and addresses methodologic issues as they arise in the protocol, including development of statistical methodology for clinical evaluations of imaging.

5.2 Master's Level Biostatistician

During protocol development, the master's level biostatistician assists the protocol statistician with sample size calculations, serves as first line of contact with the Data Management Center, works with data management to develop forms, reviews plans for web-based forms to be sure that all fields have proper range and logic checks, develops and maintains a local copy of the study database at the BDMC, develops software for database management, and develops software to do cross-form logic checks on data in the database.

When the protocol is active, the biostatistician prepares reports for teleconference calls and meetings, prepares and submits Clinical Data Update System (CDUS) reports, works with the protocol statistician to prepare reports for the DSMC, performs the majority of statistical computing for interim and final data analyses, and contributes to preparation of reports on findings from statistical analyses.

5.3 Project Manager

During protocol development, the project manager helps coordinate teleconference calls and establish guidelines for the necessary requirements for the trial (such as applications and imaging credentialing). He/she develops a study-specific budget with

the Trial PI to determine per-case monies. As part of the development of the protocol, the project manager assists in creating the Protocol-Specific Application (PSA) and other informational documents pertaining to the site application process as needed.

In preparation for trial activation, the project manager works with sites to ensure that they complete the necessary requirements for study participation: ACRIN contract, the General Qualifying Application (GQA), Federalwide Assurance (FWA), Form FDA 1572, ACRIN Statement of Investigator, the PSA, NCI Protecting Human Research Participants training (or equivalent), and the case-reimbursement schedule, as appropriate, as well as meeting all other requirements for study entry.

5.4 Coordinating and Staff Data Managers

During protocol development, the coordinating data manager assists in the review and critique of the developing protocol, the development of protocol data collection forms, and the initiation of data QA and collection procedures. Data managers prepare and supervise schema creation and develop procedures (such as validations, data checks, summary reviews, and data review tools) that maintain integrity and accuracy of the computer data files for the projects assigned. Data managers also direct, oversee, and check the process for creating the computer record for new studies. They participate in the education and orientation of new ACRIN Headquarters personnel and of clinical RAs and investigators at participating institutions. Finally, they assist in the organization and creation of education programs, activities, and written resource material, and maintain the tools (such as education manuals and Power-Point presentations) used for such activities for additional training throughout the trial.

When the protocol is active, data managers conduct ongoing review of medical data to monitor compliance, omissions, and inconsistencies, and they request correction and clarification of discrepancies. Data managers also interact with clinical investigators and RAs by telephone and through email regarding protocol procedures, data submission, data QA, eligibility, and study compliance. Data managers create special procedures for monitoring and extracting data that are not routinely computer-maintained, and they update the PIs on accrual and data issues related to the protocol.

5.5 Protocol Associate (or Medical Writer, if applicable)

During protocol development, the protocol associate (or medical writer, if applicable) assists the Protocol Team in developing the protocol, informed consent form template, and appendices. In addition, the protocol associate ensures that all sections are complete, consistent, and adhere to regulatory requirements, including those of informed consent per [NCI recommendations](#). The protocol associate maintains the master protocol documents, incorporating revisions from each investigator and other Protocol Team members. The protocol associate also helps develop the protocol timeline for use by the Protocol Team and updates it as necessary. In the case of an intergroup trial, the protocol associate will work with the other group's protocol development department to ensure that all the requirements for both groups are included in the protocol. Once the protocol is complete and the Trial PI has given

final approval for submission, the protocol associate submits it to the NCI/CTEP and ACR IRB (or other appropriate regulatory agencies) for review and approval.

Once the protocol is approved, the protocol associate distributes the protocol to participating sites and provides instructions for regulatory requirements for study participation (such as local IRB approvals). Once the protocol is active, the protocol associate coordinates revisions to the protocol, subsequent submissions for review and approval, and distribution of approved protocols (amendments and/or administrative updates per Section 8 of the [*NCI Investigator's Handbook*](#)) to the participating sites.

5.6 Regulatory Specialist

During protocol development, the regulatory specialist reviews the protocol to ensure regulatory compliance, including but not limited to: all aspects of Human Subjects Protections, International Conference of Harmonisation, Good Clinical Practice, and adherence to Code of Federal Regulation and other federal and international guidelines throughout the trial design.

5.7 Monitor(s)

During protocol development, a regulatory specialist known as the trial monitor works with the Site PIs to ensure that the site-specific informed consent form documents meet all regulatory requirements. The monitor oversees the regulatory aspects of opening the study, including submission of site activation regulatory documents (such as Site PI application materials), development of a regulatory binder, and adherence to protocol. Once the protocol is activated, and throughout the trial, the monitor advises the Protocol Team about any regulatory issues that arise. After sites accrue a specified number of participants, the monitor will request source documentation or conduct a site visit to monitor the conduct and adherence of the site to the protocol.

5.8 Auditor(s)

During protocol development, the auditors assist the Trial PI in writing study-specific audit guidelines that detail acceptable source documentation. They also provide audit education to Site PIs and RAs. Once the protocol is activated, the auditors conduct site audits to ensure data integrity and regulatory compliance. They also ensure that, whenever possible, an ACRIN physician participates in each audit.

5.9 Imaging Specialist

During protocol development, the imaging specialist works with the Trial PI and other imaging experts to identify the imaging needs of the study (e.g., reader-study specifications, technical parameters, image-quality parameters, a study-specific Imaging Management Plan). The imaging specialist will assist in development of objective criteria and metrics used to monitor study-specific images: A) on site, B) upon receipt at ACRIN Headquarters, and C) for image-quality audits. The imaging specialist assists the Trial PI in defining “minimum performance standards” and action levels with respect to positioning, noise levels, technical quality, and artifacts. The imaging specialist is responsible for routine monitoring of the images submitted

to ACRIN based on these parameters, as well as communication to sites should problems be identified.

The imaging specialist, along with other ACRIN Core Laboratory staff, will work with the Trial PI and other investigators to develop QA forms to be used at each stage/time point of imaging in the protocol. For protocols that require images to be reviewed by a radiologist or physicist for QA purposes, quick and effective image review will be considered in the forms design.

Once the protocol is activated, the imaging specialist oversees the collection and archiving of images and related reader forms. They follow the protocol design to review incoming image quality, and provide feedback and assistance to the site imaging technologist when the minimum performance limits are approached.

When the protocol is closed to accrual, the imaging specialist may assist with the imaging requirements for reader studies. Imaging specialists assigned to a specific trial may be required to attend central reader study sessions to conduct training as appropriate, monitor reader study conduct, and assist reader radiologists in the protocol-specified process.

5.10 Patient Advocate

The patient advocate represents the concerns of the participant. During protocol development, the patient advocate participates in teleconference calls and reviews the developing protocol and informed consent form(s). Once the protocol is active, the patient advocate provides suggestions to the team about advertising and recruitment.

5.11 Recruitment Specialist (if applicable)

During protocol development, a recruitment specialist may work with the Trial PI to make sure recruitment concerns are adequately addressed in the protocol, including in the PSA. Prior to trial opening, a recruitment specialist may work with the Protocol Team to determine recruitment communication strategies and related materials and to coordinate development of materials. Once the protocol is active, the recruitment specialist provides support to sites for their recruitment efforts.

5.12 Quality Assurance Committee Liaison

During protocol development, the QA Committee liaison consults with the Protocol Team to ensure data and image quality issues have been considered and incorporated into the protocol design. Once the protocol is active, the QA Committee liaison continues to consult with the Trial PI and the Protocol Team about issues relating to quality in clinical research. The QA Committee liaison may have multiple roles in the trial's conduct.

5.13 Intergroup Liaison (if applicable)

Only in cases of intergroup collaborations: During protocol development, the Trial PI must identify an intergroup liaison to coordinate work between the groups. The protocol associate and project manager also will act to coordinate needs between the

groups to ensure timelines are discussed, contracts are finalized, expectations are clear, and deadlines are met.

5.14 Other Experts (as appropriate)

During protocol development, the Trial PI should identify any co-investigators (such as pathologists, medical oncologists, epidemiologists, economists, or physicists) who will provide needed expertise to the trial team both while the protocol is being written and while the trial is accruing. These individuals also assist in the development of forms and processes for the implementation of the secondary studies.

6.0 SPECIAL CONSIDERATIONS IN TRIAL PROTOCOL DEVELOPMENT

Once a trial concept has been approved by the ACRIN Steering Committee and CTEP (and/or other regulatory agency), the Trial PI and Protocol Team will develop the trial design further using the ACRIN protocol template. The appropriate template will be sent to you via e-mail from the protocol associate assigned to the trial. This initial protocol draft will already contain components of the trial developed during concept development. The initial protocol draft will contain instructions about how to complete each section and requests for specific Protocol Team members to address components/sections of the protocol.

The following are special considerations to keep in mind when writing an ACRIN protocol.

6.1 Imaging Parameters Considerations

The Trial PI must be available to assist in the development of a trial-specific Imaging Management Plan. The staff at ACRIN needs to be properly prepared to meet the needs and requirements of a study. As the study concept is being developed, and more intensely after your study concept is approved, you will need to work with the core lab to define the technical requirements and parameters of the study early in development.

Be sure to describe:

- The type of study (prospective or retrospective);
- The imaging modalities used;
- The imaging parameters needed for trial consistency and quality assurance;
- Site readiness requirements (such as test cases or site qualification);
- Image quality control (QC) and evaluation (see Section 6.3 below);
- Image data information to be extracted/collected;
- IT requirements (such as specific workstations or software); and
- Image archiving.

From study conceptualization, if you know a particular trial endpoint will necessitate specialized software or equipment, or if you will need the core lab's assistance determining what will be required, discussions should be initiated immediately at the time of concept development to expedite the process of obtaining the necessary tools.

The Trial PI is responsible for developing procedures and requirements for local and/or centralized reader studies, including parameters requirements, training, reader study monitoring, software, and platform needs.

6.2 Image Submission Considerations

The requirements of the imaging modality or modalities used in a study need careful thought and planning. As part of your trial, the imaging data will be collected, archived, and prepared for various technical evaluation requirements at the ACR Clinical Research Center in Philadelphia, PA, which includes ACRIN staff and the ACR Core Lab.

6.2.1 Recommended Image Data Guidelines for ACRIN Trials

- ACRIN implements the TRIAD system to automate and facilitate DICOM exchange processes between participating institutions and the ACRIN image archive. ACRIN encourages you to work with your institution's IT department and ACRIN to introduce this system for image transfer. For additional details, contact the ACRIN core lab at Triad-Support@acr-arrs.org and visit the TRIAD Learning Center at <https://triad-promise.acr.org/Learning.htm>.
- All image data should arrive at ACRIN in DICOM format (contact the core lab for instructions). DICOM file headers are a requirement for all studies that require quantitative measurement outputs. When DICOM-formatted digital image data are not submitted, additional resources are required for translation and conversion into DICOM-file format and may impact the structure, end points, and budget for the study. Again, contact the imaging core lab to ensure appropriate anonymization and translation.
- If for some reason the TRIAD system cannot be introduced at sites or imaging requirements limit the use of the TRIAD system, then CDs, DVDs, or films are an option.
- We highly recommend that any image evaluations required for your study be done centrally at ACRIN Headquarters. If distributed and remote readings are required, evaluation will need to be completed with regard to available imaging systems designated for this purpose.

6.3 Image Quality Control Considerations

During protocol development, it is important for you to consider imaging QC processes. QC methods should be outlined in the protocol and may include the submission of phantom or test cases or approval of sites' initial images to ensure compliance with the protocol requirements. You and the core lab will develop the methods for images QC. The site qualification PSA also may contain questions that ascertain the ability of sites to provide images of adequate quality.

Related forms—including an Image Transmittal Worksheet (ITW) that must accompany each case—will be developed, collected, and distributed to ACRIN imaging specialists or other reviewers as appropriate to assess quality. Once images are submitted to ACRIN, an imaging specialist in the core lab will QC the images to ensure they conform to protocol-specific guidelines. As required per protocol, the imaging specialist may distribute the images to the radiologist or physicist responsible for overall QA of the study images for a timely review. As appropriate, the radiologist or physicist will communicate the results of his/her findings to the core lab imaging specialist and/or acquiring institution's PI or physicist. If the images pass QC and QA inspections, they will be held in the ACRIN Imaging Archive until radiologist review for study-related purposes.

6.4 Participant Accrual Considerations

As you work on your ACRIN protocol, keep in mind study-specific accrual needs and challenges. As you are designing the protocol's procedures, carefully consider what

the participant is being asked to do during the course of the trial. Design the trial to minimize obstacles to participant recruitment, especially: limit the number of additional procedures and/or days into the health care facility, include timelines with flexibility for the participant and the sites' scheduling needs, consider the burden of study-related procedures in addition to standard of care, and take into account the participants' possible disease burden. The protocol should specify site recruitment goals and provide the number of participants (or acceptable range) expected per site over a certain time period. The protocol also should detail what steps will be taken if those accrual goals are not met.

You will work with the ACRIN project manager and/or recruitment specialist, as applicable, to develop questions for your protocol's PSA that address recruitment. Such questions will define how participants will be recruited for this trial and help determine the ability of potential sites to recruit.

Once the protocol is approved by CTEP, and/or other regulatory agency as appropriate, you will work with ACRIN staff, possibly including a recruitment specialist, to develop strategies for participant recruitment. Recruitment preparation may include the production of recruitment communication materials (such as brochures, flyers, and letters to referring physicians). Recruitment materials should be made available to interested sites in sufficient time for local IRB approval prior to the site's opening for accrual. Once the study is open to accrual, as Trial PI you will have responsibility for contacting Site PIs at institutions that are having difficulty accruing in order to understand the nature of the accrual barriers and, with the help of ACRIN personnel, to suggest strategies to improve participant recruitment.

6.5 Biostatistics and Data Management Considerations

As Trial PI, you will work with the Biostatistics and Data Management Center (BDMC) to develop the statistical component of the trial and the case report forms (CRFs) for collecting your trial data. The Trial PI works with the protocol statistician and his/her staff to develop the statistical section for the protocol, including plans for interim and/or final analyses and sample size computations. As you work on developing CRFs, keep the following points in mind:

- Use existing templates as much as possible. The lead protocol data manager (DM) will provide templates of standardized forms and copies of applicable forms from previous studies. If you have forms from similar research or use of similar technology, please provide them to the DM to facilitate inclusion of routine data elements for your specialty.
- Think about the data points being collected and how they relate to the study's endpoints. Is the data necessary for *this* trial or "nice to have"?
- Be mindful of the complexity of the CRFs and the time required to complete them. Failure to use standard data elements from the ACRIN database and the inclusion of complex questions will slow the development of CRFs, place additional burden on participating sites, and limit the ability for ACRIN researchers to review data across multiple studies. In addition, long and complex forms may present a barrier to participant accrual and general study QC.

- Is the secondary aim appropriate for this trial, or should it be its own trial? Consider the overall number of secondary aims (and limit them) and how secondary studies (such as cost-effectiveness, tissue banking, and quality of life) will fit into the flow of the main study. Consider their impact on the development of the study and the completion of the primary aims, as well as their total cost/benefit.
- Consider the rigidity of eligibility criteria. Will waivers be allowed for certain laboratory or test values included as inclusion or exclusion criteria? Can the sites revert to institutional standards for certain criteria, or do we need to specify certain values as Human Subjects Protection measures? If a Site PI requests a waiver to certain criteria, would it be allowed? If so, could the criteria be opened up to anticipate this scenario?
- Consider acceptable time points, allowance for timing variations to reduce protocol variations while ensuring procedures are appropriately timed, and leeway for visit completion to accommodate scheduling and other site and participant needs. Think about the acceptable time allowable between registration and imaging, imaging and interpretation, imaging and treatment, etc.

All study tools and CRFs are required to be completed and tested prior to activation of any study.

6.6 Adverse Events Considerations

The protocol template contains a section about AEs. As Trial PI, you must assist in the development of and review the expected AEs listings for each modality/treatment being used and for investigational modalities and procedures. For trials involving INDs and interventional trials, the Trial PI may be required to act as a medical monitor for AEs and DSMB/DSMC reporting. Trial PIs may assist in developing descriptions of possible effects from the study modalities, investigational agents, and/or procedures in laymen's terms for inclusion in the informed consent form. Possible effects should be listed as likely, less likely, rare, or rare but serious.

6.7 Monitoring and Audit Considerations

Both Trial and Site PIs may be required to participate in an ACRIN audit as reviewers if funding is available.

ACRIN uses monitoring and site audits as an integral part of its QA program. The major objective of the ACRIN monitoring and audit programs is protection and welfare of human subjects. Secondly, these programs are designed to verify study data that could affect the interpretation of study endpoints. For detailed information about the ACRIN monitoring and audit programs, please see the ACRIN Regulatory Resources page online at www.acrin.org/pdrc.aspx. The Trial PI works with monitors and auditors to finalize monitoring and auditing plans for participating sites, including details of source documentation and timing of monitoring and audits.

7.0 CANCER THERAPY EVALUATION PROGRAM TERMINOLOGY

As part of the NCI, CTEP acts as a sponsor of clinical research and reviews the status of each clinical trial on an ongoing basis. The following are terms that CTEP uses to define the protocol status. An update (initiated by ACRIN PDRC using the [Protocol Status Update](#) form from CTEP) must be sent to CTEP at each trial milestone as defined below:

- **Active:** Trial is open to accrual.
- **Temporarily Closed to Accrual:** Trial is temporarily not accruing.
- **Temporarily Closed to Accrual and Treatment:** Trial is temporarily not accruing and patients are not receiving therapy or imaging.
- **Closed to Accrual, Patients Still on Treatment:** The protocol has been closed to patient accrual. Patients are still receiving therapy or imaging.
- **Closed to Accrual, All Patients Have Completed Treatment:** The protocol has been closed to patient accrual. All patients have completed therapy or imaging, but are still being followed according to the primary objectives of the study. No additional investigational agents are needed for this study.
- **Completed:** The protocol has been closed to accrual, all patients have completed therapy or imaging, and the study has met its primary objectives. A final study report/publication has been submitted to CTEP. The minimal data requirements for this final study report include total accrual, adverse drug experiences, and study results to date.
- **Administratively Completed:** The protocol has been completed prematurely (e.g., due to poor accrual, insufficient drug supply, IND closure). The trial is closed to further accrual, and all patients have completed protocol treatment or imaging. A final study report is not anticipated.
- **Publication Citation:** This form may also be used to inform CTEP of published trial results or publications in press.

8.0 ACRIN ADMINISTRATIVE INFORMATION

8.1 Contracts and Honoraria

As Trial PI, you will sign a contract with ACRIN and receive an annual honorarium so long as your trial is in development or open. You will receive your contract once the trial concept has been approved by the ACRIN Steering Committee. However, variations in funding and regulatory approvals impact the timeline. You will need to familiarize yourself with ACRIN's Conflict of Interest Statement and sign the Conflict of Interest Response Form (see Appendix 2).

8.2 ACRIN Contact Information

Up-to-date contact information for ACRIN staff is always available on the ACRIN web site at www.acrin.org/contactus.aspx. If you need assistance in reaching staff at ACRIN Headquarters, you can call the ACR Clinical Research Center in Philadelphia at the main ACRIN number: 215-574-3183. In addition to the main ACRIN web site, you may also consult the web site of the Biostatistics Center at Brown at <http://stat.brown.edu>, or call their main number at 401-863-9759.

The following list gives ACRIN departments and the structure of Protocol Team staff:

Administration—Project Managers, Project Assistant, Communications Group

Biostatistics Center—Protocol Statistician, Biostatisticians

Data Management—Data Managers

Imaging Department—Imaging Specialists

Protocol Development and Regulatory Compliance Department—Regulatory Specialist, Protocol Associate, Medical Writer, Regulatory Specialist, Monitors, Auditors

PART III: APPENDICES

APPENDIX 1: LINKS TO ONLINE RESOURCES

General

ACRIN Staff Contact Information: www.acrin.org/contactus.aspx

ACRIN History: www.acrin.org/acrin_history.aspx

Food and Drug Administration (FDA): www.fda.gov

National Cancer Institute (NCI): www.cancer.gov

Cancer Therapy Evaluation Program (CTEP): <http://ctep.cancer.gov>

Cancer Imaging Program (CIP): <http://cip.cancer.gov>

Code of Federal Regulations (CFR): www.gpoaccess.gov/cfr

Office for Human Research Protections (OHRP): www.hhs.gov/ohrp

CTEP Investigator Handbook: <http://ctep.cancer.gov/handbook>

ACRIN Protocol Development

Protocol Summary Table: www.acrin.org/currentprotocols.aspx

Protocol Development and Regulatory Resources: www.acrin.org/pdrc.aspx

- ACRIN Adverse Events Reporting Manual
Informed Consent Form Checklist
- Preliminary Concept Development
- Protocol Concept Submission (for submission to CTEP)
- Study Staff Signature and Responsibilities Log

CTEP Forms, Templates, and Documents: <http://ctep.cancer.gov/forms/default.htm>

- Protocol Submission Worksheet
- Protocol Status Update
- LOI Submission Form
- Concept Submission Form
- Amendment Request Submission Checklist
- Cost Estimate Worksheet

ACRIN Site Activation

Application Materials: www.acrin.org/applicationmaterials.aspx

- General Qualifying Application
- ACRIN Username and Password and Reader ID Request Form
- Form FDA 1572
- ACRIN Statement of Investigator

Image Quality Assurance Questionnaires, By Imaging Modality (CT, MRI, PET, and Ultrasound): www.acrin.org/applicationmaterials.aspx

ACRIN Policies

Publications Policy: www.acrin.org/PublicationsPolicy.aspx

Data Access Policy: www.acrin.org/DataAccessPolicy.aspx

If an IND agent is involved in the trial, research staff may be required to complete a Confidentiality Agreement prior to receiving the Investigator's Brochure for the agent (see Appendix 2 for the Conflict of Interest Policy and Response Form).

HIPAA Policy:

www.acrin.org/RESEARCHERS/POLICIES/HIPAAPOLICY/tabid/75/Default.aspx

Clinical/Investigational Agent Ordering Forms

Agent Management Guidelines: http://ctep.cancer.gov/branches/pmb/agent_management.htm

CTEP Forms, Templates, and Documents: <http://ctep.cancer.gov/forms/default.htm>

- Clinical Agent Request Form NIH-986
- NCI Investigational Drug Accountability Record Form
- NCI Transfer Investigational Agent Form
- NCI Return Investigational Agent Form

APPENDIX 2: AMERICAN COLLEGE OF RADIOLOGY CONFLICT OF FINANCIAL INTEREST IN RESEARCH POLICY (V.12.16.08)

Chancellors, officers, committee or commission members, staff, volunteers, investigators and all others representing or acting on behalf of the American College of Radiology (ACR) should avoid conflicts of interest or the appearance of conflicts of interest. All decisions and actions considered or made by such individuals should be based solely on the best interests of the ACR and in accordance with applicable federal, state, and local laws and regulations. Personal considerations should not be a factor in any action or decision made on behalf of the ACR. The confidence that members of the profession and the public have depends on the integrity of those who represent the ACR.

Conflict of Financial Interest in Research

As a recipient of National Institutes of Health (NIH) grant funds, the American College of Radiology is subject to the NIH requirement for grantees and investigators to comply with the requirements of 42 CFR Part 50, Subpart F, "Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought." In the handling of all such grant funds the ACR will take steps to ensure that the Investigator and any other persons responsible for the design, conduct or reporting of all research funded by PHS, or proposed for such funding will not be biased by any conflicting "significant financial interest." For purposes of this policy and in compliance with Section 50.603 of the regulation "Investigator" means Principal Investigator and includes the Investigator's spouse and dependent children. This provision applies to all persons representing or acting on behalf of the ACR (including individuals engaged in RTOG, ACRIN or other specific ACR research activities).

What Constitutes a Conflict of Interest?

A "significant financial interest" is defined as anything of monetary value in excess of \$10,000 and derived from consulting fees, honoraria, other payments for service, equity interests (or in excess of 5% ownership) or intellectual property rights. In reaching the \$10,000 or 5% equity ownership threshold the aggregated amounts from an Investigator and his/her immediate family are considered. 42 CFR Section 50.603 provides further information regarding what does and does not constitute a significant financial interest.

Disclosure

Disclosure of a significant financial interest is required when the Investigator makes application to participate in the research supported by NIH funds. A form will be provided by the ACR to the Investigator for this purpose. The form will be completed by the Investigator and returned to the ACR. This disclosure requirement is considered an "on-going" obligation of the Investigator, requiring submission of the appropriate documentation should his/her financial interests change during the course of the research. At a minimum, the Investigator will be required to complete and submit to the ACR a new conflict of interest form annually or a new assurance form from the institution.

All financial disclosure forms will be reviewed by the administrator of the research activity (i.e., ACRIN, RTOG) involved with guidance from ACR legal counsel. Any identified significant conflicting financial interests will be reviewed with the affected Investigator and reported to NIH within 60 days of its discovery by the ACR (but not the nature of the interest or other details) and actions to manage, reduce or eliminate the conflict of interest will be taken by the administrator of the research activity involved with advice from legal counsel and included in the report to NIH. All financial disclosure forms and any actions taken by the ACR to resolve conflicting significant financial interests will be recorded and kept on file in accordance with Section 50.604(e) of the regulation.

Institutions through whom investigators provide services to the ACR shall provide ACR with a written assurance that the Institution is compliant with the conflict of interest requirements of 42 CFR 50, Part F and all institutions must provide ACR with a copy of their most current conflict of interest policy. Institutions must also notify ACR of any identified conflicts of interest and if an Institution has identified an Investigator as failing to comply with the Institution's conflict of interest policy and such failure has biased the design, conduct or reporting of PHS-funded research the Institution must promptly notify ACR of any corrective action taken or to be taken.

Such notification to ACR is necessary so that ACR can consider the situation, comply with its reporting obligations to NIH, take appropriate action or refer the matter back to the Institution for further action, including instructions to the Institution on how to maintain appropriate objectivity for the funded project.

Conflict of Interest Disclosure Forms

In addition to the above guidance, formal Conflict of Interest disclosure forms will be required from the following groups of individuals on an annual basis or at the commencement of a research activity:

- Group leadership (i.e., ACRIN, RTOG)
- Scientific and support committee chairs
- All clinical trial investigators
- Data and Safety Monitoring Committee members
- Research consultants
- Speakers at ACRIN, RTOG or other ACR research meetings

Management and Enforcement

Management and enforcement of this policy is the responsibility of the administrator of the research activity (i.e., ACRIN, RTOG) affected with involvement from the respective Clinical Chair and ACR Executive Director. In the case of reported significant financial conflicting interests such actions to manage, reduce or eliminate the conflict of interest may include, but are not limited to, public disclosure of the conflict of interest, restriction on the equity involved (such as placing a stock in escrow or in a trust during the period of time of the research), limiting the role of the Investigator, divestiture of the financial interest or severance of the relationship that is the source of the conflict of interest.

Any significant conflict of financial interest not reported but discovered during the course of a research activity will be immediately investigated by the administrator of the research activity involved with assistance from ACR legal counsel. Reporting to NIH will be in accordance with the guidance described above. Depending upon the nature of the conflict of financial interest and the facts surrounding the failure of reporting in accordance with 42 CFR Part 50, Subpart F, corrective action to manage, reduce, or eliminate the conflict of interest will at a minimum include consideration of those actions described above. In addition, ACR may take more punitive action such as elimination of the Investigator and/or the Institution involved from further participation in ACR research activities.

Notice

All institutions and individuals providing or engaged in research activities for the ACR will be provided with a copy of this policy.

V.12.16.08



CONFLICT OF INTEREST RESPONSE FORM

In accordance with ACRIN policy, you serve in a role which requires you to complete this response form. Do you or any immediate family member have **either** a relationship or financial interest in excess of \$10,000 with any business, organization or other activity that may conflict or appear to conflict with your duties, responsibilities or exercise of independent judgment in any transaction or matter involving ACRIN?

YES _____ NO _____

If you answered "YES" please describe the nature of the relationship or financial interest in excess of \$10,000 for any activity, investment or compensation you received for a single activity.

A conflict does not necessarily imply that an individual is ineligible to serve in the assigned role. A conflict may, however, limit participation on specific activities.* Financial conflicts of interest over \$10,000 must be reported to the NCI. During the course of your participation on ACRIN activities any change in your status that would constitute a conflict or potential conflict must be reported to the ACRIN Administrator or ACRIN Chair.

ACKNOWLEDGMENT

I acknowledge that I have read and understand the above requirements for reporting any potential or actual conflicts of interest during my tenure with ACRIN.

Name: _____
(Print) (Signature)

Date: _____

Please return to:
ACRIN Administration
1818 Market Street
Suite 1600
Philadelphia, PA 19103
Phone: (215) 574-3183 Fax: (215) 717-0936

*This information is taken from the ACRIN Policy on Conflict of Interest. The full text of the policy is found on the ACRIN web site at www.acrin.org.

APPENDIX 3: ACRIN TELECONFERENCE CALLS

Because ACRIN is a virtual network, many important decisions are made on teleconference calls. As an ACRIN Trial PI, you are responsible for leading these calls. As an ACRIN Site PI, you are responsible for attending these calls or ensuring the attendance of an appropriate designee. Staff at ACRIN Headquarters will help Trial PIs develop call agendas. ACRIN staff will also take minutes and distribute reminders, minutes, and agendas.

During the concept and protocol development process, teleconference calls are usually small and involve only the Protocol Team. These calls are a forum for developing the protocol and refining other logistical issues involving the study. At this stage of development, the team will discuss and formalize the key processes of the study.

During pre-activation and activation, the calls usually expand to involve Site PIs and RAs so that they can be informed about important study information. Some studies alternate holding calls for only the Protocol Team and holding calls for all sites involved in the study; this approach allows the Protocol Team to discuss issues that may not be appropriate for a wider group.

Sometimes Trial PIs have concerns or questions about ACRIN operational issues. Those issues are appropriate to discuss on either a call for only the Protocol Team or an off-line discussion with ACRIN staff. If such issues come up on a general call for all sites, it is appropriate for the Trial PI to discuss them off-line with ACRIN staff and then inform the sites of the resolution. If necessary, the Trial PI and ACRIN staff can appoint a smaller working group that can investigate the issue and present their resolution to the larger group.

APPENDIX 4: SITE PREPAREDNESS AND ONGOING TRIAL PROCEDURES CHECKLISTS

SITE PI CHECKLIST 1: INITIAL TRIAL PARTICIPATION REQUIREMENTS

This checklist is a guide for ACRIN Site Principal Investigators (PIs) who take responsibility for the conduct of the research and adherence to a specific protocol at an ACRIN-qualified institution. It describes the initial requirements for participating in an ACRIN trial. *Although a Site PI may designate research staff to assist with some of these requirements, ultimately the Site PI is responsible for ensuring that all initial and ongoing participation requirements are met according to the guidelines outlined in the study-specific protocol. For additional details of these requirements, see Part I of the ACRIN Principal Investigator's Manual.*

ACRIN Initial Trial Participation Requirements		
ADMINISTRATIVE REQUIREMENTS	Done	Completion Date
General Qualifying Application (GQA)	<input type="checkbox"/>	
<i>The site has submitted a General Qualifying Application (GQA) to ACRIN administration, and it has been approved by the Institutional Participants Committee (IPC).</i>		
ACRIN Contract	<input type="checkbox"/>	
<i>The Site PI and appropriate institutional official(s) have completed an ACRIN contract and returned it to ACRIN administration.</i>		
Protocol Specific Application (PSA)	<input type="checkbox"/>	
<i>The site has determined it has the required imaging hardware and software, qualified personnel, and capability to recruit the anticipated number of participants as described in the protocol and has submitted a Protocol Specific Application (PSA) to ACRIN administration.</i>		
Case Reimbursement Schedule	<input type="checkbox"/>	
<i>The Trial PI has completed the study-specific case reimbursement schedule with ACRIN Project Manager; note when you receive it at the site.</i>		
REGULATORY REQUIREMENTS	Done	Completion Date
ACRIN Statement of Investigator and/or Form FDA 1572	<input type="checkbox"/>	
<i>The Site PI has completed and submitted to ACRIN administration an ACRIN Statement of Investigator and/or Form FDA 1572, along with the current CVs (signed and dated) and copies of medical licenses, as appropriate, for all personnel listed on the Statement of Investigator and/or Form FDA 1572.</i>		

ACRIN Initial Trial Participation Requirements		
Human Research Education	<input type="checkbox"/>	
<i>All institutional staff participating in the trial has completed the NCI Protecting Human Research Participants module, or other approved education to qualify them to work with human subjects. Documentation of completion has been faxed to ACRIN administration.</i>		
OHRP Assurance	<input type="checkbox"/>	
<i>The Site PI or appropriate institution staff has faxed a copy of the institution's current OHRP-issued Federalwide Assurance (FWA) to ACRIN administration.</i>		
Informed Consent Form and IRB Approval Letter Submission	<input type="checkbox"/>	
<i>The site has modified the informed consent form template in the CTEP-approved protocol to make it site-specific and has submitted it—along with the protocol and any communications and recruitment materials—to their local IRB or Ethics Committee for approval. Upon approval, documents are delivered to ACRIN PDRC.</i>		
IND-Trial Documentation	<input type="checkbox"/>	
<i>If necessary, the site has filled out and submitted to ACRIN a confidentiality agreement and conflict of interest statement (see Appendix 2) in order to obtain the Investigator's Brochure for the IND agent.</i>		
Health Insurance Portability and Accountability Act (HIPAA)	<input type="checkbox"/>	
<i>The site has addressed issues related to the Health Insurance Portability and Accountability Act (HIPAA) per the policies of the institution and/or local IRB.</i>		
SITE READINESS REQUIREMENTS	Done	Completion Date
Lead Research Associate Identification	<input type="checkbox"/>	
<i>The Site PI has identified a lead RA, preferably someone with clinical research experience, who will be dedicating time to the trial.</i>		
Site Staff Work Flow and Study Site Signature and Responsibility Log	<input type="checkbox"/>	
<i>The site has identified how the trial will be conducted among institutional departments involved in recruitment and all trial procedures. The Site PI and RA have discussed workflow, including the involvement of other physicians, departments, and shared staff, and scheduled regular meetings. Participating clinicians and research staff have received their appropriate delegations of responsibility for the trial. Delegations have been recorded on the Study Site Signature and Responsibility Log and have included their signatures for Good Clinical Practice, trial management, and auditing purposes.</i>		
Institutional Support/Services	<input type="checkbox"/>	
<i>The Site PI is aware of the infrastructure his/her institution provides for research support/services.</i>		
Initial Education	<input type="checkbox"/>	
<i>The Site PI and RA have received initial education by attending ACRIN trial-specific training sessions and meetings, participating on teleconference calls, and attending any other required informational sessions conducted by the Trial PI, ACRIN, or product manufacturers.</i>		

ACRIN Initial Trial Participation Requirements		
Password/Reader ID Forms	<input type="checkbox"/>	
<i>The Site PI, RA, and other members of the research team who will be responsible for entering data on the ACRIN web site have completed the ACRIN Username and Password and Reader ID Request Form and received confirmation of their individual passwords. Every research staff member must have his or her own password, which acts as the individual's electronic signature per 21 CFR Part 11 compliance. Passwords must not be shared with other staff members.</i>		
Review of Manuals	<input type="checkbox"/>	
<i>The Site PI has reviewed the ACRIN manuals: this Principal Investigator's Manual, the Audit Manual, and the Adverse Events Reporting Manual.</i>		
Study-Specific Requirements	<input type="checkbox"/>	
<i>The Site PI has ensured that any other study-specific requirements are met (such as submission of test cases, scanner qualification, etc.).</i>		
Recruitment Plans	<input type="checkbox"/>	
<i>The Site PI and RA have developed patient recruitment plans, including complying with local IRB requirements and/or working with the institution's public relations department, if feasible, to promote awareness of the study within the institution and community.</i>		
IMAGING REQUIREMENTS	Done	Completion Date
Imaging Team Responsibilities	<input type="checkbox"/>	
<i>The Site PI is responsible for the overall conduct of the imaging for the trial, and may designate imaging components to appropriate research staff and imaging specialists. Each member of the site imaging team should have responsibilities defined in the Study Site Signature and Responsibility Log prior to initiation of the trial.</i>		
Dedicating Scanner Time for Research	<input type="checkbox"/>	
<i>The Site PI is responsible for establishing time for research on an ACRIN-qualified scanner and is responsible for the overall adherence of the site to protocol-specific parameters.</i>		
Image Submission	<input type="checkbox"/>	
<i>The Site PI implements processes for imaging completeness and timely submission of images to ACRIN for the protocol and has coordinated those processes with the institutional IT department as necessary.</i>		
ACRIN Personnel Visit	<input type="checkbox"/>	
<i>If applicable, imaging personnel from ACRIN may visit the site to configure equipment for image transfer and conduct on-site training.</i>		
Quality Assurance and Quality Control Processes	<input type="checkbox"/>	
<i>The Site PI is aware of the ACRIN quality assurance (QA) processes for the entire trial and 100% quality control (QC) review of images. Once aware of QA and QC measures for the trial, site will be able to comply with them.</i>		

SITE PI CHECKLIST 2: ONGOING TRIAL PARTICIPATION REQUIREMENTS

This checklist describes the ongoing requirements for participating in an ACRIN trial. For additional information, see Section 12 of the [NCI Investigator's Handbook](#), "The Organization of a Clinical Trial." If you have questions about any of these items, please contact ACRIN Headquarters.

ACRIN ONGOING TRIAL PARTICIPATION REQUIREMENTS	
<input type="checkbox"/>	ACRIN Reports and Reminders
<i>The Site PI or designated research staff responds promptly to all reports received from ACRIN Headquarters (forms due reports, data queries, IRB approval expiration notices, etc.).</i>	
<input type="checkbox"/>	Adherence to Protocol and Monitoring/Audit Preparation
<i>The Site PI ensures that his/her own site adheres to protocol procedures; is prepared for site monitoring and site audit; and follows up promptly with any of the audit team's recommendations.</i>	
<input type="checkbox"/>	Adverse Events Reporting
<i>The Site PI is responsible for the reporting of all adverse events, especially serious adverse events, in compliance with ACRIN and NCI-Cancer Imaging Program, Food and Drug Administration, or other regulatory review board policies.</i>	
<input type="checkbox"/>	Staff Oversight
<i>The Site PI meets with the RA(s) and any other research staff on a regular basis to ensure that the clinical research is being conducted appropriately according to the protocol, images of adequate quality are being produced, and all forms and responses to ACRIN queries are being submitted to ACRIN in a timely manner.</i>	
<input type="checkbox"/>	ACRIN Statement of Investigator and/or Form FDA 1572
<i>The Site PI is ultimately responsible for ensuring all regulatory documentation specific to IND trials (e.g., Form FDA 1572, Study Site Signature and Responsibility Log) is updated, current, and submitted to ACRIN as necessary. Any changes to Section 6 (related to subinvestigators) of the Form FDA 1572 and/or to Section 2 of the ACRIN Statement of Investigators will need to be submitted to ACRIN. (Each updated document will need to be signed and dated by the investigator prior to submission to ACRIN.) Personnel changes will need to be documented on the Study Site Signature and Responsibility Log.</i>	
<input type="checkbox"/>	For IND Trials: Coordinating Agent Orders, Storage, and Administration
<i>The Site PI ensures investigational agents are available, stored, and administered per DCTD (see Sections 9, 14, and 15 of the NCI Investigator's Handbook) and protocol-specific guidelines.</i>	
<input type="checkbox"/>	Local IRB Interaction
<i>The Site PI ensures that all protocol amendments and requests for ongoing study approval are submitted to the local IRB, and all approval documentation is sent to ACRIN PDRC in a timely manner.</i>	

ACRIN ONGOING TRIAL PARTICIPATION REQUIREMENTS	
<input type="checkbox"/>	Teleconference Call Participation
<i>The Site PI or a PI-designated representative is present on all required teleconference calls.</i>	
<input type="checkbox"/>	ACRIN Meeting Attendance
<i>The Site PI(s) and RA(s) attend ACRIN meetings as requested.</i>	
<input type="checkbox"/>	Participant Accrual Monitoring
<i>The Site PI and RA(s) monitor participant accrual progress and report any specific recruitment barriers to the Trial PI.</i>	
<input type="checkbox"/>	Recruitment Plans
<i>The Site PI and RA(s) comply with participant recruitment plans and modify recruitment procedures as necessary to improve distribution of communication materials, educational sessions at departmental meetings, regular contact with referring physicians, etc.</i>	
<input type="checkbox"/>	Imaging Quality Assurance (QA)
<i>The Site PI and/or designated staff members comply with all required ongoing imaging QA processes.</i>	
<input type="checkbox"/>	Requesting Waivers to Eligibility and Other Protocol Requirements
<i>The Site PI requests approval via the Trial PI for a waiver to eligibility criteria or other protocol requirements. The Site PI must await final approval from the ACRIN Network Chair prior to proceeding with registration or the procedure.</i>	