

**American College of Radiology
Imaging Network**

PRINCIPAL INVESTIGATOR MANUAL

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PREFACE

This manual is designed for American College of Radiology Imaging Network (ACRIN) Principal Investigators (PIs). There are two sections: the first section, for site/protocol PIs, details the requirements for participating in an existing ACRIN trial, while the second section, for trial PIs, contains information about ACRIN protocol development and implementation. 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 ACRIN Procedure Manual, the Adverse Events Reporting Manual, and the Audit Manual, all of which contain more detailed information about these topics. This manual also supplements the more general Investigator's Handbook (<http://ctep.cancer.gov/handbook/>) developed by the Cancer Therapy Evaluation Program (CTEP) of the National Cancer Institute (NCI).

ACRIN is a National Cancer Institute Clinical Trials Cooperative Group made up of investigators from over 100 academic and community-based medical facilities in the United States and Canada. The goal of ACRIN is to conduct clinical trials that improve the health, longevity, and quality of life of cancer patients through the use of diagnostic imaging and image-guided treatment procedures.

Over 45 ACRIN staff members provide administrative, data management, statistical, quality assurance, and protocol development support for group investigators. The administrative staff and data management staff (which is under the direction of the Biostatistics Center) are headquartered in the ACR Clinical Research Office in Philadelphia. The Biostatistics Center is located at Brown University in Providence, Rhode Island. ACRIN receives funding from the National Cancer Institute as well as corporate and foundation support.

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SITE PRINCIPAL INVESTIGATORS

SITE PI CHECKLIST: INITIAL TRIAL PARTICIPATION REQUIREMENTS

This checklist is a guide for ACRIN site/protocol Principal Investigators (PIs). 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.*

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

ACRIN Initial Trial Participation Requirements		
Administrative Requirements	Done	Completion Date
1. General Qualifying Application (GQA)	<input type="checkbox"/>	
<p><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></p> <p>Once the GQA has been approved, ACRIN is responsible for sending the site a contract. Sites that have already 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: www.acrin.org/institutions.html. The GQA is available on that web page. If you have questions about the GQA, please contact ACRIN Administration.</p>		
2. ACRIN Contract	<input type="checkbox"/>	
<p><i>The site PI and appropriate institutional official have completed an ACRIN contract and returned it to ACRIN administration.</i></p> <p>Please note that an institutional contract may already be in place if an institution has previously participated in ACRIN trials. 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.</p>		
3. Protocol Specific Application (PSA)	<input type="checkbox"/>	
<p><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></p> <p>PSAs are on the ACRIN web site at www.acrin.org/institutions.html. All PSAs must be approved by the ACRIN Institutional Participants Committee (IPC).</p>		
4. Case-Reimbursement Schedule	<input type="checkbox"/>	
<p><i>The site PI has completed the study-specific case reimbursement schedule.</i></p> <p>The case reimbursement schedule will be sent out to all sites by ACRIN administration.</p>		

ACRIN Initial Trial Participation Requirements		
5. Statement of Investigator	<input type="checkbox"/>	
<p><i>The site PI has submitted an ACRIN Statement of Investigator and a current CV to ACRIN administration.</i></p> <p>The ACRIN Statement of Investigator is available on the ACRIN web site at www.acrin.org/pi.html and as Appendix 3 of this manual.</p>		
Regulatory Requirements	Done	Completion Date
6. Human Research Education	<input type="checkbox"/>	
<p><i>All institutional staff participating in the trial have completed the Office of Human Research Protections (OHRP) module or other approved education to qualify them to work with human subjects, and have faxed documentation of this to ACRIN administration.</i></p> <p>The OHRP module is available at http://ohsr.od.nih.gov. If your institution requires a different course, please contact ACRIN administration to determine whether that course is sufficient.</p>		
7. Office of Human Research Protections (OHRP) Assurance	<input type="checkbox"/>	
<p><i>The PI or RA has faxed the ACRIN Protocol Development and Regulatory Compliance Department a copy of the institution's current OHRP-Issued Federal Wide Assurance, Multiple Project Assurance, or Cooperative Project assurance.</i></p> <p>This information is available from your institution's IRB. Alternatively, researchers may search for their institution at http://ohrp.osophs.dhhs.gov/irbasur.htm, then print out that documentation and fax it to ACRIN (215-574-0300). Please see Section IV of the ACRIN Procedure Manual for more information about assurances.</p>		
8. Consent Form and IRB Approval	<input type="checkbox"/>	
<p><i>The site has modified the informed consent form template in the protocol to make it site-specific and has submitted it—along with the protocol and any communications and recruitment materials—to their local Institutional Review Board (IRB) or Ethics Committee for approval.</i></p> <p>Sites must modify the informed consent form template to make it specific for their institution. Sites may reword and expand the consent, but they must not delete sections. If a local IRB requests extensive revision of the consent form, please contact the ACRIN Protocol Development and Regulatory Compliance Department for guidance. Please see Appendix 5 for the ACRIN Informed Consent Checklist.</p>		
9. IRB Documentation	<input type="checkbox"/>	
<p><i>The site has faxed the IRB approval letter and a copy of the approved institutional informed consent form, along with the ACRIN Informed Consent Checklist, to the ACRIN Protocol Development and Regulatory Compliance Department.</i></p> <p>Please fax the documentation to 215-574-0300. The site will not be able to accrue participants onto a trial until this documentation has been entered into the ACRIN database.</p>		

ACRIN Initial Trial Participation Requirements		
10. 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>		
Please note that ACRIN does not monitor HIPAA compliance. Sites may incorporate the HIPAA authorization in their consent or keep it separate. They may use their own authorization or they may use ACRIN's template. More information about ACRIN's HIPAA policy, as well as ACRIN's HIPAA authorization template authorization, is available at http://www.acrin.org/hipaa.html .		
Site Readiness Requirements	Done	Completion Date
11. Research Associate Identification	<input type="checkbox"/>	
<i>The site has identified a research associate (RA), preferably with clinical trials experience, who will be dedicating time to this trial.</i>		
RAs will receive information and education from ACRIN about ACRIN procedures and the specific protocol, 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.		
12. Site Staff Work Flow	<input type="checkbox"/>	
<i>The PI and RA have discussed workflow and scheduled regular meetings.</i>		
Clear communication between PI and RA is crucial. Ultimately, the site PI is responsible for the conduct of the trial at the institution.		
13. Institutional Support	<input type="checkbox"/>	
<i>The PI is aware of the infrastructure his/her institution provides for research support.</i>		
Contact your institution's research office for more information. It is important to know what resources are available to you.		
14. Initial Education	<input type="checkbox"/>	
<i>The PI and RA have received initial education by attending ACRIN meetings, participating on conference calls, and attending any other required informational sessions conducted by the study PI or product manufacturers.</i>		
The PI and RA will be notified of general ACRIN and study-specific informational sessions.		
15. Password/Reader ID Forms	<input type="checkbox"/>	
<i>The PI, RA, and other members of the research team who will be responsible for entering data on the ACRIN web site have completed ACRIN Username Request Forms and received confirmation of their individual passwords.</i>		
This form is available as Appendix 2 to this manual. Every research staff member must have his or her own password; ACRIN requires that passwords not be shared.		

ACRIN Initial Trial Participation Requirements		
16. Review of Manuals	<input type="checkbox"/>	
<p><i>The site PI has reviewed the ACRIN manuals: this Principal Investigator Manual, the Audit Manual, the Adverse Events Reporting Manual, and the Procedure Manual.</i></p> <p>These manuals will be sent upon request to investigators interested in participating in ACRIN trials; they are also available on the ACRIN web site (http://www.acrin.org/resources.html).</p>		
17. Study-Specific Requirements	<input type="checkbox"/>	
<p><i>The site PI has ensured that any other study-specific requirements are met (such as submission of test cases, PET credentialing, etc.).</i></p> <p>These requirements are protocol-specific and will be detailed in the PSA and in the individual protocols.</p>		
18. Recruitment Plans	<input type="checkbox"/>	
<p><i>The PI and RA have determined patient recruitment plans, including working with the institution's public relations department, if feasible, to promote awareness of the study within the institution and community.</i></p> <p>Recruitment plans should be in place before accrual begins. Sites can work with ACRIN's recruitment specialist to develop those plans. Some institutions also offer valuable public relations resources for clinical trials.</p>		
Imaging Requirements	Done	Completion Date
19. Image Submission	<input type="checkbox"/>	
<p><i>The site PI has put in place processes for image submission for this protocol and has coordinated those processes with the institutional IT department.</i></p> <p>Imaging requirements vary by protocol and are delineated in detail in the protocol. It is important to be aware of your institution's IT processes and policies.</p>		
20. ACRIN Personnel Visit	<input type="checkbox"/>	
<p><i>If applicable, imaging personnel from ACRIN have visited the site to configure equipment for image transfer.</i></p> <p>This requirement is protocol-specific. You will be contacted by ACRIN if this is necessary. If applicable, an equipment contract must be signed.</p>		
21. Quality Assurance (QA) Processes	<input type="checkbox"/>	
<p><i>The site PI is aware of the quality assurance (QA) processes for this protocol and will be able to comply with them.</i></p> <p>QA processes are specific to each protocol and will be found in the protocol itself or in a separate study-specific manual.</p>		

SITE PI CHECKLIST: ONGOING TRIAL PARTICIPATION REQUIREMENTS

This checklist describes the ongoing requirements for participating in an ACRIN trial. If you have questions about any of these items, please contact ACRIN headquarters.

ACRIN ONGOING TRIAL PARTICIPATION REQUIREMENTS

1. ACRIN Reports and Reminders

The site PI 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 PI designates his/her staff to respond, the PI should make sure that the designee responds promptly.

2. PI Audit Participation

The site PI takes the ACRIN Online Physician Audit Training Module and attends at least one site audit.

All site investigators are required to attend at least one site audit. Travel expenses will be reimbursed by ACRIN.

3. Audit Preparation

The site PI ensures that his/her own site is prepared for a site audit and follows up promptly with any of the audit team's recommendations.

Detailed information about ACRIN audit requirements can be found in the ACRIN Audit Manual (on the web at www.acrin.org/resources.html) and either in the auditing section of the protocol or in a separate set of study-specific audit guidelines.

4. Adverse Events Reporting

The site PI oversees the reporting of all adverse events in compliance with ACRIN and NCI-Cancer Imaging Program policies.

Detailed information about ACRIN adverse events reporting requirements can be found in the ACRIN Adverse Events Reporting Manual (on the web at www.acrin.org/resources.html) and in the adverse events section of the protocol.

5. Staff Oversight

The site PI meets with the RA or RAs and any other research staff on a regular basis to ensure that the protocol is being conducted appropriately and images of adequate quality and all forms are being submitted to ACRIN in a timely manner.

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

ACRIN ONGOING TRIAL PARTICIPATION REQUIREMENTS**6. Local IRB Interaction**

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 in a timely manner.

Amendments will be circulated to site PIs and RAs via e-mail. That e-mail will specify whether expedited or full board review is required. All studies must also be reviewed annually by the local IRB, and documentation must be faxed to the ACRIN Protocol Development and Regulatory Compliance Department. If the IRB approval is listed as “expired” in the ACRIN database, the site will not be allowed to accrue.

7. Conference Call Participation

The site PI or a PI-designated representative is present on all required conference calls.

Important information about the conduct of the study is conveyed on the conference calls. Calls also offer opportunities for PIs and RAs to ask questions and share challenges they are facing with the trial.

8. ACRIN Meeting Attendance

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

The fall ACRIN meeting is open to all ACRIN investigators, and all site PIs and RAs are encouraged to attend protocol-specific and general sessions. The spring meeting is by invitation only; those PIs and RAs who are invited will be notified in advance by ACRIN headquarters.

9. Recruitment Plans

The site PI and RA implement participant recruitment plans to include distribution of communication materials, educational sessions at departmental meetings, regular contact of referring physicians, etc.

Recruitment issues will be discussed on conference calls and at ACRIN meetings. When possible, ACRIN will provide assistance with the development of communication materials.

10. Participant Accrual Monitoring

The site PI and RA monitor participant accrual progress and report any specific recruitment barriers to the trial PI.

Sites are encouraged to work with the ACRIN recruitment specialist and the study PI if they have any questions or concerns.

11. Imaging Quality Assurance (QA)

The site PI and/or designated staff members comply with all required ongoing imaging quality assurance processes.

The study-specific quality assurance procedures vary by modality and are detailed either in the protocol or in a separate study-specific manual.

TRIAL PRINCIPAL INVESTIGATORS

ACRIN CONCEPT SUBMISSION AND PROTOCOL DEVELOPMENT

The principal business of ACRIN is the conduct of rigorous, multi-institutional multidisciplinary clinical trials. Although ACRIN provides the financial support necessary to conduct its own trials, ACRIN is not a funding agency. Rather, it provides a centralized infrastructure for the conduct of trials and includes among its functions protocol design; biostatistical services; data and image transmission, storage, and management; the development and maintenance of standards; quality assurance; and data analysis. Investigators recruited by ACRIN to conduct its trials 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.

- 1. An idea for a trial is proffered 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 a Disease Site Committee

- 2. The idea is considered by the appropriate Disease Site 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. The Disease Site 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.

- 4. The individual appointed by the Disease Site Committee to be responsible for concept development presents the preliminary concept to the ACRIN Steering Committee for preliminary approval.**

The Steering Committee decides whether to move forward with further development of the concept based on whether the concept is consonant with the Network'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.

5. Concepts approved by the Steering Committee undergo further development and submission as more complete concepts to the Cancer Therapy Evaluation Program (CTEP).

The Disease Site Committee will add members to the Trial Team, including naming a Trial PI. The Trial Team adds detail to the concept prepare it for submission to CTEP. Concepts submitted to CTEP must use the ACRIN Protocol Concept Submission Template.

6. Following the recommendation by CTEP, the Steering Committee makes a final determination of whether it will pursue protocol development and open the trial.

The principal consideration is whether ACRIN has the financial resources and personnel required.

7. The Trial Team, Biostatistical and Data Management Center, and Headquarters collaboratively develop a timeline for future activities and assign roles and responsibilities to members of the protocol team.

8. The Trial Team develops the protocol, including recommendations made by CTEP and submits the protocol for CTEP approval.

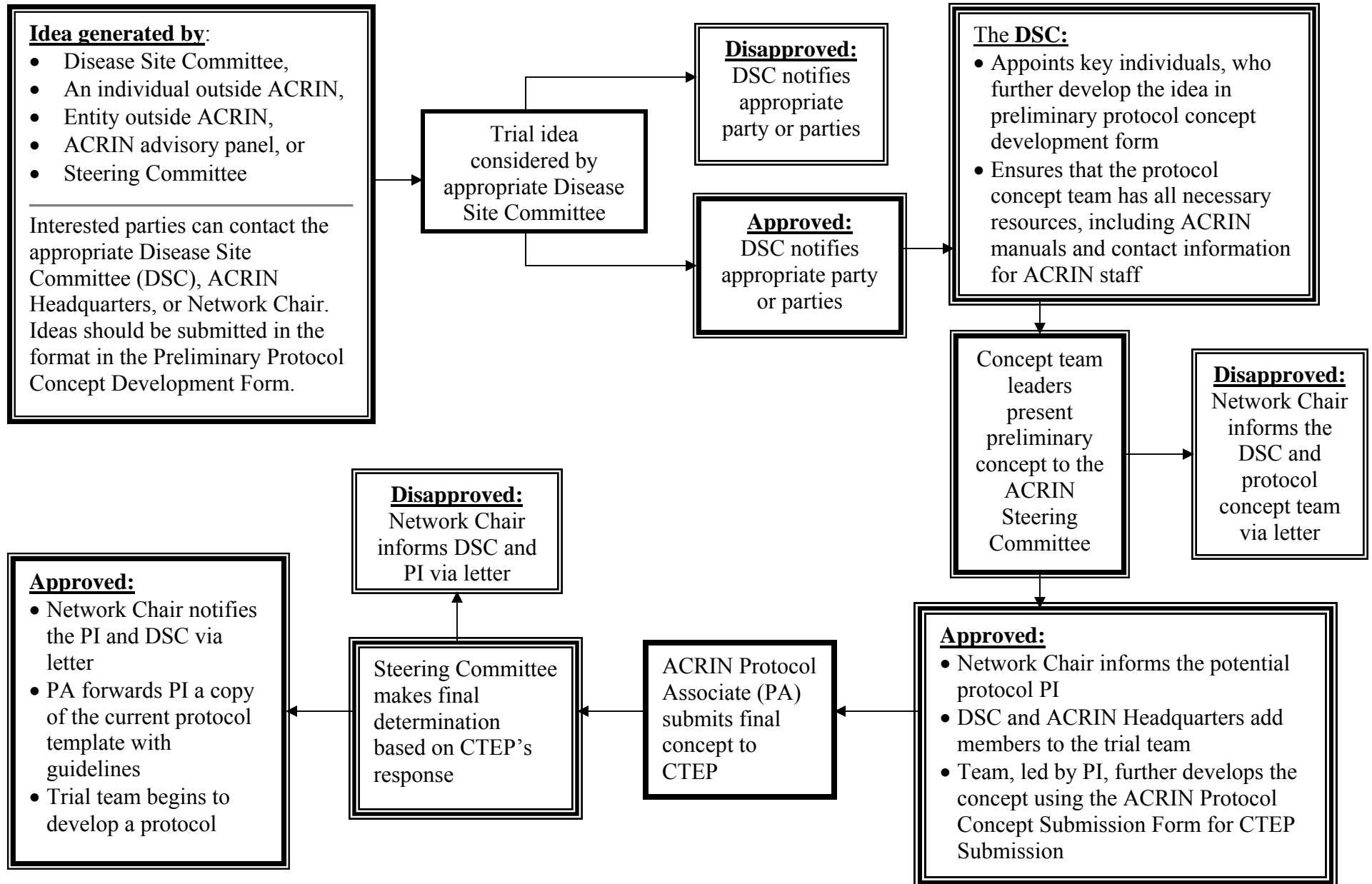
Trial Teams should include the PI, additional imaging and non-imaging specialists who are experts in the disease site and technologies represented in the trial, statisticians, other methodologists, Headquarters project manager, regulatory, data management, and audit personnel, a patient advocate, and such other experts as are necessary to develop a rigorous protocol.

The team, led by the PI, begins to develop the protocol using the ACRIN protocol template with guidelines (sent electronically to the PI). Once a draft of the protocol is completed, the protocol team reviews it fully. A revision based on that review is then sent simultaneously to the ACRIN Quality Assurance (QA) Committee and the protocol team for final review. At that point, the protocol associate makes any final edits and submits the protocol to the Cancer Therapy Evaluation Program for review and comments. The protocol is then either approved outright or returned with comments. If comments are returned, the team revises and resubmits until CTEP approves the protocol. The protocol must also be approved by the ACR IRB; that submission may be simultaneous with CTEP submission. During the approval and comment response interaction, if not earlier, protocol specific forms must be finalized.

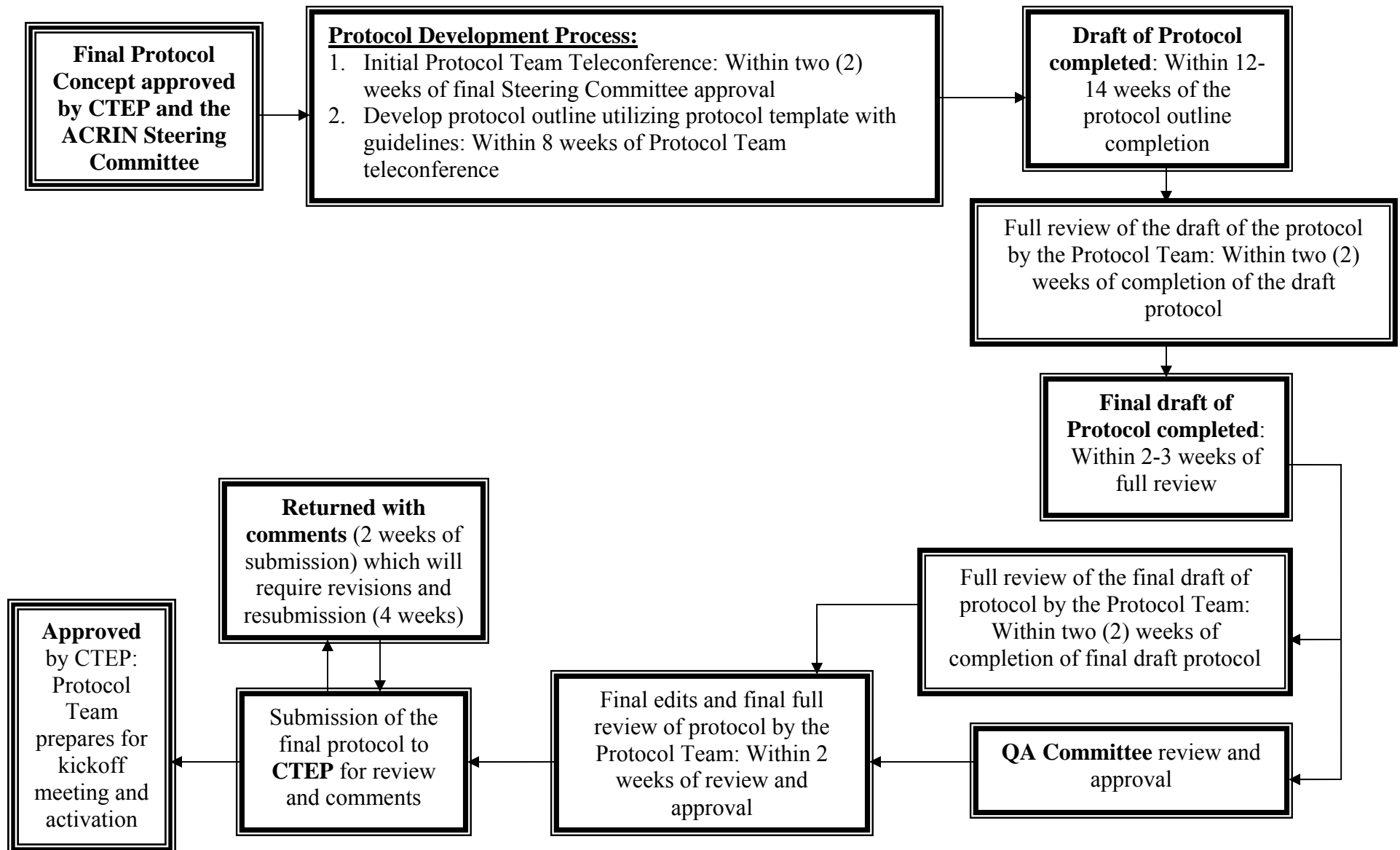
9. CTEP approves the protocol and the trial opens.

Once the protocol is approved, participating sites must submit the protocol to their IRBs for approval and receive any necessary hardware and software. Contracting between institutions and ACRIN or addenda to existing contracts are also finalized during this period. At that point, the protocol team, led by the PI, begins planning the kickoff meeting for research associate and investigator education. After the kickoff meeting, the protocol is activated and sites may begin accruing.

ACRIN CONCEPT DEVELOPMENT AND SUBMISSION PROCESS



ACRIN PROTOCOL DEVELOPMENT PROCESS AND TIMELINE



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 Investigator's Handbook (<http://ctep.cancer.gov/handbook/>) developed by the NCI's Cancer Therapy Evaluation Program.

During Protocol Development:

- Leads and assists in the development of protocol, protocol-specific application, and data collection forms
- Interacts with the outcomes experts, statisticians, and other methodologists as required for protocol development and analysis
- Assists in establishment and implementation of quality assurance of images
- Interacts with key experts related to establishment of standardization of technical parameters of protocol images
- Assists in the development, detailing, and implementation of reader studies
- Assists in coordinating the piloting of data forms prior to study activation
- Assists ACRIN headquarters staff in developing a budget, selecting sites, and developing and monitoring the protocol development timeline
- Assists 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
- Interacts with participating site PIs and the ACRIN recruitment specialist to promote patient recruitment
- Assists in planning the operational aspects of the protocol and its related secondary studies

While Protocol Is Active:

- In collaboration with the study statistician, leads the work on monitoring study progress, including accrual, data collection, and data monitoring
- Answers protocol-specific eligibility and protocol procedure questions
- Undergoes ACRIN audit education and attends at least one site audit
- Assists in establishment of target accrual goals for participating sites and works with ACRIN recruitment specialist to develop specific patient recruitment strategies
- Continues planning any reader studies

Throughout Development and Activation:

- In collaboration with personnel at ACRIN headquarters, develops the agenda and leads the discussions on protocol-specific conference calls
- Provides reports and updates on protocol to the ACRIN Steering Committee as requested
- Attends all ACRIN Semi-Annual Meetings; dictates minutes from meetings to include action items and highlights
- Presents the status of the trial at semi-annual meetings when requested and leads meeting sessions devoted to protocol development, implementation, and ongoing needs
- Plans and leads a kickoff meeting to prepare site PIs and RAs for the activation of the protocol
- Follows up with PIs at sites not meeting accrual goals to assess accrual barriers and develops and monitors a remedial plan to improve accrual
- Notifies disease site and/or modality committee chairs and Steering Committee via written communication should trial accrual fall under 75 percent of the expected accrual rate at any point after the trial reaches one quarter of the expected accrual time; the written communication will document the accrual barriers and plans for addressing the barriers
- Participates in meetings of the Data and Safety Monitoring Committee and responds to DSMC questions and concerns

After Study Closes to Accrual:

- Continues to work with the protocol team, other investigators, and participating sites to follow up participants and ensure adequate data collection
- Works with protocol team on implementing sub-analyses and the initiation of reader studies
- Works with the Biostatistics and Data Management Center to clean up the data
- Organizes and leads the work on preparation of manuscripts for publication

MEMBERS OF THE PROTOCOL TEAM

In addition to the Principal Investigator, the following people compose the protocol team: the protocol statistician, the master's level biostatistician, the project manager, coordinating and staff data managers, the protocol associate, the regulatory specialist, the patient advocate, the intergroup liaison (if applicable), the imaging specialist, the recruitment specialist, the auditors, the QA Committee liaison, 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 conference calls and preparation of documents) is provided by ACRIN Headquarters.

See below for a description of the duties of each member of the protocol team.

- **Protocol Statistician:** During protocol development, the protocol statistician works with PI to refine study aims, determine study design and primary endpoint(s), and establish operating procedures for the study, including quality assurance. The protocol statistician also determines adequate study size and plans interim and final analyses.

When the protocol is active, the protocol statistician oversees Biostatistics and Data Monitoring Center (BDMC) work on monitoring patient accrual and data collection and quality, coordinates data analyses, coordinates 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.

- **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 Biostatistics Center, 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 conference calls and meetings, submits Clinical Data Update System (CDUS) reports, works with protocol statistician to prepare reports for the Data Safety and Monitoring Committee (DSMC), performs the majority of statistical computing for interim and final data analyses, and contributes to preparation of reports on findings from statistical analyses.

- **Project Manager:** During protocol development, the project manager helps coordinate conference calls and helps establish guidelines for the necessary requirements for the trial (such as applications and imaging credentialing).

He/she will also work with the PI in the development of a study specific budget that includes per case monies. As part of the development of the protocol, the project manager will also assist in creating the protocol-specific application and other informational documents pertaining to the application process as needed. In preparation for 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), the Protocol-Specific Application (PSA), and the case-reimbursement schedule, as well as meeting all other requirements for study entry.

- **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 quality assurance procedures and data collection. 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 also participate in the education and orientation of new headquarters personnel and of clinical research assistants and investigators. Finally, they assist in the organization and creation of education programs, activities, and written resource material and develop and maintain the headquarters tools (such as education manuals and Power-Point presentations) used for such activities.

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 research associates by telephone and through email regarding protocol procedures, data submission, data quality assurance, eligibility, and study compliance. Data managers create special procedures for monitoring and extracting data that are not routinely computer-maintained, and they update the PI on accrual and data issues related to the protocol.

- **Protocol Associate:** During protocol development, the protocol associate assists the protocol team in developing the protocol and ensures that all sections are complete and consistent. 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, the protocol associate submits it to the ACR IRB and the Cancer Therapy Evaluation Program (CTEP) of the National Cancer Institute for review. Once the protocol is approved, the protocol associate distributes the protocol to participating sites and works with them to make sure regulatory requirements for study participation (such as OHRP assurances and IRB approvals) have been met. Once the protocol is active, the protocol associate coordinates revisions to the protocol and distributes approved protocols and any amendments to the participating sites.

- **Regulatory Specialist:** During protocol development, the regulatory specialist works with the PI to ensure that the protocol meets all regulatory requirements, including those for the informed consent. The regulatory specialist also oversees the regulatory aspects of opening and closing the study. Once the protocol is activated, the regulatory specialist advises the protocol team about any regulatory issues that arise.
- **Auditors:** During protocol development, the auditors assist the 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.
- **Imaging Technology Specialist:** During protocol development, the imaging technology specialist works with the PI to identify the imaging needs of the study and image quality parameters, which must be monitored. The imaging technology specialist will assist in development of objective criteria and metrics used to review images A) on site, B) upon receipt at ACRIN headquarters, and C) for image quality audits. The Imaging Specialist would assist the PI in defining “minimum performance standards” and action levels with respect to positioning, noise levels, technical quality and artifacts.

The imaging technology specialist, along with the Image Management Center (IMC) staff, will work with the PI in the development of the quality assurance forms to be used at each stage in the protocol. For protocols that require images to be reviewed by a radiologist or physicist for quality assurance, assistance will be given in the design of forms for quick and effective image review.

Once the protocol is activated, the imaging technology specialist oversees the collection and archiving of images and related reader forms. They follow the protocol design for incoming image quality review, and provide feedback and assistance to the site technologist when the minimum performance limits are approached. When the protocol is closed to accrual, the imaging technology specialist may assist with the imaging requirements for any reader studies.

- **Patient Advocate:** During protocol development, the patient advocate participates in conference calls and reviews the developing protocol and consent form. The advocate represents the concerns of the participant. Once the protocol is active, the patient advocate provides suggestions to the team about advertising and recruitment.
- **Recruitment Specialist:** During protocol development, the recruitment specialist works with the PI to make sure recruitment concerns are adequately addressed in the protocol, including in the protocol-specific application (PSA). Prior to trial opening, the recruitment specialist works with 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.

- **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 PI and the protocol team about issues relating to quality.
- **Intergroup Liaison (if applicable):** If this will be an intergroup trial, during protocol development the PI must identify an intergroup liaison to coordinate work between the two groups.
- **Other Experts (as appropriate):** During protocol development, the 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 it is accruing. These individuals also assist in the development of forms and processes for the implementation of the secondary studies.

WRITING AN ACRIN PROTOCOL: SPECIAL CONSIDERATIONS

Once your concept has been approved by the ACRIN Steering Committee and CTEP, you will develop it further using the ACRIN protocol template, which will be sent to you by e-mail. That template contains instructions about how to complete each section. In addition, the following are issues to keep in mind when writing an ACRIN protocol.

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 Philadelphia office of the ACR. In order for the staff at ACRIN to be properly prepared to meet the needs and requirements of this study, after your study concept is approved the Image Management Center (IMC) will send you the Image Requirements Questionnaire (see Appendix 4). This questionnaire contains questions about the type of study (prospective or retrospective), the imaging modalities used, image data information, image evaluation, IT requirements (such as specific workstations or software), site readiness requirements (such as test cases or site credentialing), and image archiving. This form needs to be updated whenever the imaging information in the protocol changes.

We recommend the following general guidelines for image data for ACRIN trials:

- We recommend that the participating study institutions supply ACRIN with 1st generation digital image data direct from the modality. This image data should be in DICOM 3.0 and is a requirement for all studies that will require any type of quantitative measurement outputs. When other than DICOM 3.0 formatted digital image data is submitted it requires additional resources for translation and conversion into DICOM 3.0 file format and may impact the structure, end points, and budget for the study.
- We highly recommend that any image evaluations required for this study be done centrally at ACRIN headquarters. If distributed and remote reading is required, evaluation will need to be completed with regard to available imaging systems designated for this purpose.
- If films are to be submitted, originals should be provided whenever possible. If films must be returned to the institution they will be digitized by ACRIN for purposes of the permanent study record and returned as quickly as possible.

Image Quality Control Considerations

It is important that you consider during protocol development how imaging quality control will be ensured. Such methods may include the submission of test cases or approval of sites' initial images to ensure compliance with the protocol requirements. The Image Management Center (IMC) will develop with the Principal Investigator the methods in which the QC images and related forms will be acquired, collected, and distributed to reviewers. Once these images are submitted to ACRIN, the imaging

technology specialist along with the Image Management Center (IMC) will distribute them to the radiologist or physicist responsible for the quality assurance of these images for a timely review. After the review, the radiologist or physicist will communicate the results of his/her findings to the acquiring institution's PI or physicist. The Protocol-Specific Application may also contain questions that ascertain the ability of sites to provide images of adequate quality.

Participant Accrual Considerations

As you work on your ACRIN protocol, keep in mind study-specific accrual needs and challenges. 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 should also detail what steps will be taken if those accrual goals are not met.

You will work with the ACRIN recruitment specialist to develop questions for your protocol's protocol-specific application (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, you will work with the recruitment specialist to develop potential strategies for participant recruitment, including the production of recruitment communication materials such as brochures, flyers, and letters to referring physicians. Recruitment materials should be provided to 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.

Data Management Considerations

As trial PI, you will work with the Biostatistics and Data Management Center (BDMC) to develop case report forms (CRFs) for your protocol. As you work on developing forms, keep the following points in mind:

- Use existing templates as much as possible. The Data Management Center (DMC) will provide you copies of similar forms from previous studies.
- Think about the data points being collected and how they relate to the study's end points.
- 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 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.
- Consider 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 acceptable timepoints. Think about the acceptable time allowable between registration and imaging, imaging and interpretation, imaging and treatment, etc.
 - Data quality must be a foremost concern at each step in the process.

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

Adverse Events Considerations

Prompt reporting of adverse events (AEs) is the responsibility of each investigator, clinical research associate, and/or nurse engaged in clinical research. All ACRIN trial and site PIs need to become familiar with AE reporting as it relates to imaging trials. Please refer to the ACRIN AE Reporting Manual for detailed information about AE reporting. Whenever possible, use the terminology included in the latest version of the Common Terminology Criteria for Adverse Events (currently CTCAEv.3.0).

The protocol template contains a section about adverse events. As trial PI, you must fill in the expected adverse events for each modality/treatment being used. These expected AEs must also be mentioned in the informed consent form.

Audit Considerations

Both Trial and Site PIs are required to participate in an ACRIN audit as reviewers.

ACRIN uses site audits as an integral part of its quality assurance and regulatory compliance programs. The major objective of the ACRIN audit program is to verify study data that could affect the interpretation of primary study endpoints. For detailed information about the ACRIN audit program, please see the ACRIN Audit Manual.

A set of protocol-specific audit guidelines must contain a chart detailing acceptable source documentation for that protocol. As trial PI, you will work with the data management and the audit team to determine what source documentation will be deemed acceptable. You will also need to work with them to determine, based on the size and complexity of your protocol, the timing of the initial and subsequent audits.

Statistical Considerations

The protocol statistician and his or her staff will develop the statistical section for the protocol, including plans for interim and final analyses and sample size computations. The Biostatisticians can also provide investigators with educational material and information on the design and conduct of clinical trials. Please discuss this with the protocol statistician on your study.

CANCER THERAPY EVALUATION PROGRAM TERMINOLOGY

The Cancer Therapy Evaluation Program (CTEP), National Cancer Institute, as a sponsor of clinical trials, reviews the status of each clinical trial on an ongoing basis. The following are terms that CTEP uses:

- **Approved, Not Yet Active:** Protocol has received CTEP approval but is not yet accruing.
- **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:** The protocol has been closed to patient accrual. Patients are still receiving therapy or imaging.
- **Closed to Accrual and 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.
- **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.
- **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.

ACRIN ADMINISTRATIVE INFORMATION

Contracts and Payment

As trial PI, you will sign a contract with ACRIN and be provided an annual honorarium so long as your trial is in development or open. You will receive your contract once the trial is approved and the protocol team begins to develop the protocol. If your institution will be participating in the trial, the institution will also be provided with the case reimbursement schedule, as sent to all participating sites, for execution.

ACRIN Contact Information

Up-to-date contact information for ACRIN staff is always available on the ACRIN web site at <http://www.acrin.org/contacts.html>. If you need assistance in reaching staff at ACRIN headquarters, you can also call the ACR Philadelphia Office main number at 215-574-3150. 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 included protocol team staff:

Administration—Project Manager, Recruitment Specialist

Biostatistics Center—Protocol Statistician, Biostatisticians

Data Management—Data Managers

Imaging Department—Imaging Technology Specialist

Protocol Development and Regulatory Compliance Department—Regulatory Specialist, Protocol Associate, Auditors

APPENDICES

APPENDIX 1: ACRIN Publication Policy

1. Statement of General Principles Regarding Publications

1.1 Overall Goal:

A goal of ACRIN, in addition to conducting clinical trials research, is to disseminate results of the research to the scientific community. These results will include results of primary study outcomes, secondary analyses, and ancillary studies. Priorities in selecting journals/forums for publications submission will be given to peer-reviewed journals as well as presentations and publications of abstracts at national and international scientific meetings.

2. General Considerations

2.1 This document represents the overall publication policy of the ACRIN Clinical Trials Group and provides for some flexibility. By way of definition, a publication is any document submitted to a professional journal listed in the Index Medicus or any popular periodical.

2.2 Publication of ACRIN data undertaken without conforming to these policies is not permitted without prior written consent from the ACRIN Executive Committee.

2.3 None of the rules contained herein should be allowed to contravene the principles that: all individuals who have made substantial intellectual, scientific and practical contributions to the trial and the manuscript should, where possible, be credited as authors; all individuals credited as authors should deserve that designation. It is the responsibility of each ACRIN trial principal investigator, the Publications Committee and, ultimately, the Executive Committee to ensure that these principles are upheld.

2.4 All manuscripts resulting from ACRIN trials should be published in peer review journals.

2.5 In all cases where journal policies permit, all investigators who contribute patients to the trial will be acknowledged.

2.6 The status of manuscripts in preparation will be reviewed at each ACRIN meeting

3. Responsibilities/Role of the Publications Committee

3.1 Promote, facilitate, and monitor the timeliness of publication of ACRIN trial results.

3.2 Propose policy guidelines for authorship of publications. Update guidelines as necessary.

3.3 Assure compliance with ACRIN publication policies.

3.4 Establish standards of excellence for publications.

- 3.5 Assure authorship is correct so that appropriate contribution credit is recognized.
- 3.6 Provide peer-review of the science of abstracts and papers. Review, edit and approve all publications and presentations prior to submission, enlisting the special assistance of ACRIN modality or organ committees whenever appropriate. Reviews will be conducted pursuant to the following general editorial responsibilities:
 - 3.6.1 Ensure that all ACRIN publications preserve the scientific integrity of the study;
 - 3.6.2 Correct factual and conceptual inaccuracies, if necessary;
 - 3.6.3 Safeguard the rights of volunteer participants;
 - 3.6.4 Prepare comments to assist collaborating scientists in publishing papers of the highest quality and clarity;
 - 3.6.5 Avoid conflict with and/or duplication of other publications.
- 3.7 Review, suggest necessary revisions, and approve any publications arising from approved ancillary studies prior to their submission for publication. In addition to issues cited in the editorial policy above, proposed publications of ancillary studies will be scrutinized to ensure that their presentation or publication will not threaten the presentation/publication of results from the primary study.
- 3.8 Adjudicate disputes involving publications issues.
- 3.9 Recommend policy and procedures for review and approval of all communications (written and spoken) regarding ACRIN trials outcomes to outside groups.
- 3.10 Facilitate public dissemination of the study and coordinate press releases;
- 3.11 Track media representation of ACRIN trial results;
- 3.12 The ACRIN Headquarters will maintain an up-to-date bibliography and repository of all publications pertaining to ACRIN studies. It is the responsibility of the primary authors to provide ACRIN headquarters with the most up-to-date version of any publications. Headquarters will be responsible to providing any related documentation to the National Cancer Institute (NCI).
- 3.13 Exceptions to the Publications Rules for manuscripts, abstracts, and oral presentations may be recommended by the Publications Committee and approved by the Executive Committee.

4. Standards of Excellence

In addition to the review system established for the critique of publications and presentations, the following guidelines are suggested for maintaining the highest standards of excellence for ACRIN publications and presentations:

- 4.1 If, in the opinion of the Publications Committee, there is no member who has sufficient scientific background to review the pertinent material, then outside expert consultants will be selected by the Publications Committee and asked to critique the material.
- 4.2 For major publications and presentations, the completeness or adequacy of reports may be assessed by the following criteria:
 - 4.2.1 Purpose of the report should be clearly stated.
 - 4.2.2 Rationale for selection of the population inclusion and exclusion criteria should be explicitly delineated.
 - 4.2.3 Information should be presented on the loss of subjects during the study including reasons for loss to follow-up. Data should be presented to demonstrate comparability of the subjects who participated and who exited from each study group.
 - 4.2.4 Statement should be made regarding the effects to achieve masking to defend against the introduction of bias.
 - 4.2.5 The report should detail statistical tests employed.
 - 4.2.6 The authors should provide the pertinent results as well as the estimated range of treatment effects, i.e., use of confidence intervals in reporting results.
 - 4.2.7 There should be notation of the power to assure the reader of the strength of the conclusion, especially if a negative conclusion is reached.
 - 4.2.8 Significance testing should be used in conjunction with an empirical review of the data.

5. Publication of Primary Study Outcomes

5.1 Manuscript Preparation

- 5.1.1 All primary ACRIN manuscripts should acknowledge in the title of the paper that this is a group effort of the American College of Radiology Imaging Network (ACRIN). Each cover page should acknowledge the grant support. In addition, each publication shall include other notices as are required by Sponsors providing funding for the protocol(s) discussed in the publication and any disclaimers required by the sponsor or ACRIN.
- 5.1.2 Evaluation of the protocol records necessary for final analysis will begin when approximately 80% of the data has been collected, or if early termination of a trial is deemed appropriate. The Study Statistician and support staff will perform this review. The Study Statistician will notify the trial PI(s) when the data are sufficiently mature to warrant generation of a publication.
- 5.1.3 The trial PI(s) will write the scientific paper from the study data as first author(s). Alternatively, the trial PI may nominate to the Publications Committee a substitute for consideration as first author. Input to the manuscript will be sought from the protocol statistician(s) and other members of the trial team. The primary author will be responsible for assuring production of the draft of the paper within three months of

availability of the data. This time period should allow for review and comment of the draft by all co-authors. Following revisions, the trial PI(s) will submit the final manuscript to the Publications Committee Chair.

- 5.1.4 The Publications Committee Chair will assign appropriate members from the committee (or, when necessary, from outside the committee) to conduct the final review prior to submission for publication. Within two weeks, members of the publications committee will review the final manuscript and return comments to the primary author. The primary author is responsible for final manuscript revisions and submission to an appropriate peer review journal within 6 weeks months after receipt of the Publications Committee's review.
- 5.1.5 Final manuscripts for some trials may necessitate review by a specific manufacturer/company based on prior written agreements. It will be the responsibility of the trial PI to be aware of such arrangements and to comply with them.
- 5.1.6 Manuscripts must be completed and submitted within a reasonable period of time following the writing directive. If, after a period of three months following completion of data analysis, the draft is not substantially complete, the Executive Committee/Publication Committee reserve the right to make other arrangements to ensure timely publication. If a satisfactory manuscript is not produced within the allotted time frame, the Executive Committee/Publications Committee may reassign the manuscript. The Publications Committee may grant an extension when it is deemed necessary.
- 5.1.7 Copies of the journal reviewer's criticisms, responses and final revised manuscript will be sent to all co-authors. The primary author must keep the Publications Committee apprised of all events following submission (i.e., acceptance). Copies of the reprinted article will be sent to each co-author and maintained at the ACRIN Headquarters. Requests for copies of manuscripts will not be considered until the manuscript is in press.

5.2 Authorship

- 5.2.1 Investigators will be offered the opportunity to publish as a group or with recognition of individual authors. This decision should be made before the activation of a trial.
- 5.2.2 Membership and authorship representation for any trial resides with the participant institution. When an investigator leaves an institution, it is up to the site PI to assign someone to the authorship spot allocated for that institution. If a site PI leaves an institution, he/she maintains his/her authorship rights with the permission of the trial team, provided he/she has accessed patients to the study and continues to work with the trial team.

In situations where papers will have individual authors, the following rules will apply:

- 5.2.3 Members of the trial team (normally the trial PI(s) and up to three representatives from organ/modalities involved in the trial) will be entitled to authorship provided they have contributed patients to the trial. Principal authors of primary manuscripts of ACRIN trials will also include the trial biostatistician(s). Ordinarily, ACRIN will embrace the custom of placing the biostatistician after the primary author(s) of primary manuscripts. However, the order of the author list may be adjusted as appropriate for each manuscript. The primary author must have contributed at least 5% of the eligible cases to the study.
- 5.2.4 Additional authors will be identified from institutions who have accrued “substantial” numbers of patients to the study and who have met quality standards for data submission, as well as other contributions. A representative from each institution contributing the largest number of evaluable cases will participate as co-author. For smaller scale (or Phase II) studies, this will be limited to 2-3 institutions, but expanded to encompass 25% of the evaluable entries for larger studies. In general, “substantial” will be defined as at least 5% of accrual, and between 5-10% for smaller scale studies. The exact criterion for a given trial will depend on: 1) the total number of authors (see criterion below) and 2) the pattern of accrual by center for the trial (e.g., there may be an obvious cutoff). Only one author per institution per paper will be allowed unless a second individual made a major contribution to the ACRIN study or the institution of the first author entered at least 25% of all evaluable cases. Institutions contributing greater than 50% of evaluable cases will be permitted a total of three authors. A maximum of ten authors will be allowed for a small (100 patients or less study), or a maximum of 15 authors for a large (>100 patients) study.
- 5.2.5 An institution must meet ACRIN quality standards for continuing institutional participation for the investigator to qualify for authorship.
- 5.2.6 The principal investigator at a qualifying institution will ordinarily be the author but may defer authorship to another investigator at his/her site.
- 5.2.7 If a statistician, reviewing pathologist or other scientist has made substantial contribution to a study, he/she should be listed as a co-author. Additional authors may be named from the ACRIN Biostatistical Group based on specific contributions.
- 5.2.8 Each author is responsible for obtaining any appropriate clearances at his/her institution.
- 5.2.9 Every paper must include an appendix or table of all contributors to the study.

5.2.10 Disputes about authorship which cannot be resolved by the protocol committee will be referred to the Publications Committee.

6. Publication of Secondary Manuscripts and Ancillary Studies (Subgroup Analyses)

6.1 Concept Approval Process for Ancillary/Correlative Projects

6.1.1 Secondary papers are those in which data are examined for nonpredetermined endpoints and may cross several studies.

6.1.2 Any individual may submit a request to investigate ancillary data contained in any approved ACRIN protocol to the Research Strategy Committee. Examples of such project might be: (1) laboratory correlative studies, (2) pathology correlative studies, (3) record studies, or (4) subgroup analyses not undertaken in the primary manuscript. Preference will be given to investigators who have contributed to the primary study or to ACRIN in the past. If the request is granted, the investigator will be expected to produce a manuscript of publishable quality within 9 months, following the same principles outlined above in 5.1.3 and 5.1.4. The Publications Committee will be kept apprised of all such projects. If such a document is not produced, the Publications Committee will have the prerogative of reassigning the data to another interested individual.

6.1.3 An individual is limited to 2 requests per calendar year. Investigators who have one set of data being worked on and one pending may not submit another request.

6.1.4 Approval of ancillary or correlative projects will be determined on a case-by-case basis. When investigators not involved in the primary ACRIN trial propose such projects, the biostatistician for the primary trial will be involved in the data analysis and coordination of the ancillary project.

6.1.5 Secondary papers that are identified by the trial PI and/or Statistical Group at the time the primary paper is being written will be assigned to authors at institutions with the largest accrual.

6.1.6 A companion or ancillary study should not be reported before the principal results of the primary study are published. Development of primary manuscripts is expected to proceed in a timely manner.

6.1.7 Approval for publication or presentation of ancillary studies that may jeopardize the outcome of a primary ACRIN trial may be withheld until such time as is deemed appropriate by the Publications Committee.

6.1.8 With the exceptions noted above, all ACRIN Publications procedures and criteria apply.

6.2 Authorship of Ancillary/Correlative Projects

- 6.2.1 Authorship of manuscripts resulting from these secondary analyses of ACRIN data will be afforded to the investigators involved in the research, those with the greatest (evaluatable) patient accruals and an appropriate ACRIN statistical representative (as described above).
- 6.2.2 Authorship of manuscripts from ancillary projects will be determined based on a variety of parameters, including overall workload contribution, intellectual contribution, and participant accrual. Tentative arrangements regarding authorship should be discussed at the time of initial approvals.
- 6.2.3 In addition to manuscripts reporting the clinical trial results, there also may be methodologic papers utilizing ACRIN data. A charge of the Biostatistics Center is to develop methods for diagnostic test evaluation. Similarly, methodologic work may be done by representatives of the outcomes committee or by economists. Normally, the authors of such papers would be the methodologists who developed the particular techniques with other authors included only if they contributed intellectually to the paper. For instance, if data from a particular study are used in a methodologic study, this does not automatically entitle the members of the protocol team to co-authorship.

7. Abstracts

- 7.1 Abstracts reporting the preliminary or highlighted results of ACRIN studies will not negate the necessity of preparing a full manuscript for publication.
- 7.2 The trial team may initiate a proposal for the submission of an abstract. The trial team and the Publications Committee must approve the concept and general content of the abstract. Guidelines for abstracts and authorship will generally follow those established for manuscripts.
- 7.3 Requests for data for the abstract should be made to the Biostatistical Center early to allow for delivery of the data requested - at least 60 days, unless otherwise negotiated with the statistician.
- 7.4 The Publications Committee must receive an abstract proposed for submission to a scientific meeting at least 14 days prior to the scientific society's deadline for receipt of abstracts to provide time for review and possible revision, unless otherwise negotiated.
- 7.5 A copy of the final abstract must be distributed to each participating clinical center at least 60 days before presentation.
- 7.6 When new ACRIN results are to be presented, a presentation script (talk copy) with tables must be sent to the Publications Committee at least 4 weeks prior to the scheduled talk.

- 7.7 An abstract approved for submission is only approved for a particular meeting. If it is rejected and the author wants to resubmit it to an alternative meeting, it must be treated as a new/separate request.
- 7.8 Unauthorized or premature disclosure of data is prohibited. Reproduction or reprinting of ACRIN data by journals without the permission of the Publications Committee is prohibited.

8. Invited Presentations

- 8.1 A presentation is the delivery of information to scientific, professional or public groups, such that public dissemination might ensue through publications, press releases, etc.
- 8.2 If members of ACRIN are personally invited to present ACRIN data or to represent ACRIN, the invitation must be forwarded to the ACRIN Steering Committee as soon as possible. The Steering Committee reserves the right to accept or not accept the invitation or to suggest an alternative ACRIN representative.
- 8.3 Invited presentations requiring the submission of a manuscript/abstract involving previously unpublished ACRIN data cannot be accepted.
- 8.4 ACRIN presentations must be limited to substantive information available either in the final protocol or other published data, with no added interpretations or inferences.

9. Intergroup Studies

- 9.1 No universally accepted publication policy for intergroup studies currently exists.
- 9.2 Prior to the initiation of an Intergroup Study, members of the Steering Committee and trial team will negotiate in writing various aspects of Intergroup Study conduct. One of these will be a Publications Policy. While this will vary from situation to situation, the essential policy will be:
- 9.2.1 Primary author(s) will be the trial PI(s).
- 9.2.2 The appropriate representative of the Biostatistical Center of the Cooperative Group responsible for data management and analysis will be an author.
- 9.2.3 Institutional authorship will be awarded to Cooperative Groups in a manner proportional to case entry.
- 9.2.4 While the manuscript preparation will proceed according to the policies of the responsible Cooperative Group, the Publications Committees of each of the Cooperative Groups will monitor progress and each committee prior to submission should approve the final draft.

10. Publicity/Press Releases/Interviews

- 10.1 A press release is defined as a document given to radio, television, newspapers, popular periodicals, or scientific journals not indexed by Index Medicus. An interview is any discussion with a member of the press, a science writer, or a radio or television commentator, which in turn provides information for public dissemination.
- 10.2 Press releases and interviews should not be initiated by clinical centers. Any ACRIN investigator who plans to have a news release on any aspect of ACRIN research activities must clear the release with the Publications Committee. The Publications Committee is responsible for notifying ACRIN Headquarters of requests received and approved. Preferably, centrally prepared press releases will be prepared, reviewed and distributed to the centers. It is suggested that these prepared releases be given to the media when interviews are requested. This procedure will help ensure uniformity and accuracy in the information distributed through the media.
- 10.3 Should a clinical center be solicited for information other than that detailed above, the center should refer the soliciting party to the ACRIN Chair or the Chair of the Publications Committee.

11. Conflict of Interest Policy

- 11.1 ACRIN investigators must adhere to the ACRIN conflict of interest policy.



APPENDIX 2: ACRIN USERNAME REQUEST FORM

Institution Name	
ACRIN Institution #	

I acknowledge that I will be assigned a username and password for data entry. Use of the username and password is restricted to my use for purposes of data entry for ACRIN protocols. By my signature, I attest that I will maintain in confidence my assigned username and password.

Name				
Role (e.g., PI, Radiologist, etc.)				
E-mail Address				
Central Study E-mail Address (if applicable)				
Signature				
ACRIN Reader ID (ACRIN Use Only)				
NIH Certification	<i>attach to form</i>	<i>attach to form</i>	<i>attach to form</i>	<i>attach to form</i>

Please indicate which studies you will be participating in by checking the study number(s) below.

<input type="checkbox"/> 6651	<input type="checkbox"/> 6652	<input type="checkbox"/> 6654	<input type="checkbox"/> 6657	<input type="checkbox"/> 6659
<input type="checkbox"/> 6660	<input type="checkbox"/> 6661	<input type="checkbox"/> 6662	<input type="checkbox"/> 6663	<input type="checkbox"/> 6664
<input type="checkbox"/> 6665	<input type="checkbox"/> 6666	<input type="checkbox"/> 6667	<input type="checkbox"/> 6668	

Principal Investigator's Signature	Date of Signature

Please allow 2-3 business days to receive your username and instructions.

Send this form to:	ACRIN Administration
at fax number:	(215) 717-0936
Send password info to:	
at fax number:	

ACRIN USE ONLY

Approved By		Date	
Issued By		Date	



APPENDIX 3: STATEMENT OF INVESTIGATOR

ACRIN Protocol # _____

1. NAME AND ADDRESS OF PRINCIPAL INVESTIGATOR (Attach CV)

2. NAMES OF THE SUBINVESTIGATORS (e.g., *research fellows, residents, associates*) WHO WILL BE ASSISTING THE INVESTIGATOR IN THE CONDUCT OF THE INVESTIGATIONS(S).

3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OFF SITE CENTERS, RELATED CLINICS, IMAGING FACILITIES, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED.

4. COMMITMENTS:

I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying ACRIN except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation(s).

I agree to report to ACRIN adverse experiences that occur in the course of the investigation(s) as specified in the ACRIN Adverse Event Manual.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records as dictated by good clinical practice. These will be available for inspection in accordance with the ACRIN audit guidelines.

I will ensure that an IRB will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators.

5. SIGNATURE OF INVESTIGATOR

6. DATE

American College of Radiology Imaging Network
1818 Market Street, Suite 1600
Philadelphia, Pennsylvania 19103-3604
Phone: (215) 544-3150
Fax: (215) 717-0936

APPENDIX 4: Image Requirements Questionnaire

ACRIN Study Number: _____ Study Chair: _____
Date: _____

As part of your American College of Radiology Imaging Network (ACRIN) study, the imaging data portion of your clinical trial will be collected, archived and prepared for various technical evaluation requirements, at the Philadelphia offices of the American College of Radiology (ACR). In order for the staff at ACRIN to be properly prepared to meet the needs and requirements of this study, we require the information requested in the enclosed questionnaire. In the event a section does not apply to the protocol design, please note with a N/A (not applicable). If you do not understand a section or need help from ACR in completing the form, please contact Anthony Levering at (215) 574-3244 or Rex Welsh (215) 574-3215.

Section 1: Type of study: Prospective or Retrospective.

Section 2: Imaging Modalities utilized for this study.

Section 3: Image data information.

Section 4: Image evaluation considerations.

Section 5: Special requirements such as specific workstations or software.

Section 6: Image Archival considerations.

The following contains general guidelines regarding image data on ACRIN trials.

- 1) We recommend that the participating study institutions supply ACRIN with 1st generation digital image data direct from the modality. This image data should be in DICOM 3.0 and is a requirement for all studies that will require any type of quantitative measurement outputs. When other than DICOM 3.0 formatted digital image data is submitted it requires additional resources for translation and conversion into DICOM 3.0 file format, and may impact the structure, end points and budget for the study.
- 2) We highly recommend that any image evaluations required of this study be done centrally at ACRIN headquarters. If distributed, and remote reading is required, and evaluation will need to be completed with regard to available imaging systems designated for this purpose.
- 3) If films are to be submitted, originals should be provided whenever possible. If films must be returned to the institution they will be digitized by ACRIN for purposes of the permanent study record and returned as quickly as possible.

2a. Will institution participants be permitted to submit image data from non-participating ACRIN institutions (i.e., outside films or digital data)?

Yes (please comment): _____

No

Section 3: Image Data

Type of image data submission?

Electronic data: FTP Media (specify type ex. Optical disk, CD, DAT, DVD)

Hard copy data: Film Other (specify type) _____

Volume of data submitted (per case)?

Electronic data: FTP (Estimated number of images per exam) _____

Media (Estimated number of disks, tapes or CD's) _____

Hard copy data: Film (Estimated number and sizes of films per exam) _____

Other (specify) _____

Section 4: Image Evaluation.

Will the imaging portion of the study require one or more reader image evaluation components?

Yes *(If yes, answer the question below)*

No

How many? _____

Will a radiologist and/or other medical expert perform these image evaluations?

Yes *(If yes, answer the questions below)*

No

How many readers? _____

Over what time period will the image studies need to be read? _____

Will all of the readers evaluate all designated study cases?

Yes

No

If No, please provide comments: _____

Do you plan for the reader image evaluations to be done centrally, or de-centralized?

Centrally? Please describe: *(ex: Parallel reading sessions, number of readers present, etc.)* _____

De-Centralized? Please describe: *(ex: workstation/software requirements, etc.)* _____

If de-centralized reader evaluations will take place, how is it anticipated that image data would be distributed to readers?

Web

CD

DVD

Other *(specify)*

Section 5: Special Requirements

Will there be any specific **image display workstations** required in order to perform the image evaluation functions for the study?

Yes *(If yes, answer the question below)* No

Will the image files be in a format other than DICOM version 3.0? Yes No

If yes, comment: _____

Will there be any specific **image display software applications** required in order to perform the image evaluation functions for the study?

Yes *(If yes, answer the question below)* No

If yes, comment: _____

Will image manipulation be a requirement of this study? Yes No

If yes, comment: _____

Will there be a Region of Interest (ROI) or other analysis?

Yes *(Please describe)* No

If yes, comment: _____

Will electronic annotations be required?

Yes *(If yes, answer please describe)* No

If yes, comment: _____

Will any associated annotation, manipulation, ROI, or calculation data need to be stored for future evaluation or analysis?

Yes (If yes, please describe) No

If yes, comment: _____

Will there be a requirement for 3D reconstruction analysis or 3D statistical outputs?

Yes (If yes, please describe) No

Will there be electronic image quantitative measurements required as part of the study?

Yes No

If Yes, will the electronic image quantitative measurements be:

- Uni-dimensional
- Bi-dimensional (Cross-product)
- Area measurements
- Volumetric calculations

It is highly recommended that when electronic image quantitation is expected, the acquisition of digital data is preferred.

Comments: _____

It is highly recommended that in order for ACRIN to provide in-house image related services that digital image data be sent in the DICOM version 3.0-file format to the ACR offices when possible. Will DICOM 3.0 be made a requirement as part of the study?

Yes No

If no, comment: _____

1c. Will ACRIN be expected to store and maintain any of the image based statistical data output information? Yes (If yes, comment below) No

Comments: _____

Section 6: Image Archival Considerations

6a. Will there be any specific image archiving or storage requirements other than ACRIN standard as part of this study? Yes (If yes, comment below) No

Comments: _____

Please note any other information you would like to supply regarding the imaging portion of this ACRIN trial:

ACRIN Notes:

Name of person filling in this form: _____
Contact telephone number of person filling in this form: _____
Email address of person filling in this form: _____

Rex Welsh, Imaging Consultant
Phone: 215-574-3215
Fax: 215-928-0153
rwelsh@phila.acr.org

Anthony Levering, Imaging Coordinator
Phone: 215-574-3244
Fax: 215 - 717-0936
alevering@phila.acr.org

Charles Apgar, ACRIN Administrator
Phone: 215-574-3231
Fax: 215-717-0936
capgar@phila.acr.org

APPENDIX 5: ACRIN Informed Consent Checklist

Protocol #: _____ **Protocol Title:** _____

Investigator Name: _____ **Site #:** _____

ACRIN Informed Consent Requirements	Yes	No	N/A	Comments
1. A statement that the study involves research	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
2. An explanation of the purposes of the research	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
3. The expected duration of the subject's participation	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
4. A description of the procedures to be followed	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
5. Identification of any procedures which are experimental	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
6. A description of any reasonably foreseeable risks or discomforts to the subject	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
7. A description of any benefits to the subject or to others which may reasonably be expected from the research	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
8. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
9. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
10. For research involving more than minimal risk, an explanation as to whether any compensation is provided, and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
11. An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
12. A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Additional Elements (Required if found in the sample ACRIN Informed Consent)	Yes	No	N/A	Comments
13. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
14. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
15. Any additional costs to the subject that may result from participation in the research	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
16. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
17. A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	
18. The approximate number of subjects involved in the study	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	

Informed consent shall be documented by the use of an IRB approved written consent form, and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.

Site Specific Informed Consent Prepared by:		
_____	_____	_____
Print Name	Signature	Date

Comments: _____ _____ _____

Informed Consent Reviewed by (PI or Supervisor):		
_____	_____	_____
Print Name	Signature	Date

ACRIN Internal Use:		
_____	_____	_____
Date of Receipt of ICF	Date of Review of ICF	Signature of ACRIN Staff

APPENDIX 6: AMERICAN COLLEGE OF RADIOLOGY CONFLICT OF INTEREST POLICY (FEBRUARY 2003)

The American College of Radiology depends to a great extent on the knowledge, expertise, and efforts of members who volunteer their services, and it is desirable that as many members as possible participate in its activities. The confidence that members of the profession and the public have in radiology and radiologists depends on the integrity of those who represent the College. Chancellors, officers, committee or commission members, staff, volunteers, and all others representing or acting on behalf of the American College of Radiology 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 College 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 American College of Radiology.

What Is a Conflict of Interest?

A conflict of interest occurs whenever an individual or a member of his or her immediate family has a direct or indirect interest or relationship, financial or otherwise, that may conflict or be inconsistent with the individual's duties, responsibilities, or exercise of independent judgment in any transaction or matter involving the College.

A conflict of interest does not necessarily imply that an individual is ineligible to serve on a College committee, commission, or task force or cannot represent the College in a specific situation, but it may indicate that participation in some matters should be avoided or limited. Questions relating to whether a conflict might arise should be referred to the chair of the Board of Chancellors or the College's executive director.

Reporting Conflicts of Interest

If an individual has an actual or potential conflict of interest relating to business or transactions before the College, he or she should immediately notify the chair of his or her commission, committee, or task force or the chair of the Board of Chancellors *and* the executive director of the College. Members of the College's staff should disclose potential or actual conflicts of interests to the executive director. The executive director should disclose his own conflicts of interest to the chair of the Board of Chancellors. In making the disclosure, the individual should reveal all material facts about the conflict of interest and explain his or her relationship to the transaction or matter at issue. In some circumstances, full disclosure of the conflict may in itself be sufficient to ensure the integrity of College operations.

If a conflict of interest arises in connection with the activities of a deliberative body, such as a commission, committee, or the Board of Chancellors, the conflict should be disclosed to the other members of the body and the individual should not participate in the consideration of the matter at issue. Any withdrawal by a member of a commission, committee, or task force and the reasons for it should be recorded in the minutes of the meeting. Councilors and alternate councilors with a conflict of interest relating to a policy matter before the Council may participate in de-bate on that issue after disclosing the conflict to the Council but should refrain from voting.

When a conflict arises from an individual's presentation or participation in a seminar, workshop, or other such event, or in connection with an individual's contributions to a College publication, the facts giving rise to the conflict should be disclosed to other participants, attendees, or readers and the individual should clearly identify his or her statements or contributions as personal opinions.

**AMERICAN COLLEGE OF RADIOLOGY
CLINICAL RESEARCH CONFLICTS OF INTEREST
DISCLOSURE STATEMENT**

The intent of this disclosure statement is not to prevent a researcher with a conflict of interest from participating in research but to make known the relationship to the American College of Radiology Imaging Network (ACRIN) so the potential conflict can be evaluated. The requirements of this disclosure statement also apply to future conflicts of interest that may arise during the course of a research study.

Failure to report a conflict of interest could result in the imposition of administrative sanctions. Such sanctions may include oral admonishment, written reprimand, notification to the appropriate institutional official, suspension or termination from participation in the ACRIN.

What is a conflict of interest?

A conflict of interest may be considered to exist if an investigator or a member of his/her immediate family is "affiliated" with, or has a "financial interest" in commercial organizations that may have a direct or indirect interest in the research being conducted by the ACRIN. A financial interest may include, but is not limited to, being a shareholder in the organization; being on retainer with the organization; or having research or honoraria paid by the organization. An affiliation may be holding a position on an advisory committee, board of directors or some other role of benefit to a sponsoring organization.

The following questions apply to the investigator and his/her immediate family.

- 1) Currently or anytime within the past year did you receive any compensation from a corporation or organization in which the value of the compensation could be affected by the outcome of research in which you are involved?
Yes___No___
- 2) Currently or anytime in the past year did you have a proprietary interest in any drug, biologic product, or medical device, including but not limited to, a patent, trademark, copyright or licensing or royalty agreement?
Yes___No___
- 3) Currently or at any time in the past year did you have an equity interest in a pharmaceutical or medical equipment manufacturing company that exceeds \$25,000 in value?
Yes___No___
- 4) Currently or at any time in the past year did you or your institution receive any form of financial assistance (cash, equipment, retainers for consultation, or honoraria) in excess of \$25,000 from a single corporation or organization involved in ACRIN clinical trials in which you participate?
Yes___No___
- 5) Currently or at any time in the past year did you hold a position on any advisory committee, board of directors or other policy making position for any pharmaceutical or medical equipment manufacturing company?
Yes___No___

If you answered “yes” to any of the questions, please provide below the name of the company or organization involved and a brief description of the nature of the financial relationship.

This form must be completed annually or at any time there is a change in the nature of the financial relationship. All information provided will be kept in strictest confidence.

Name

Signature

Date

Please return this form to: **Charles Apgar**
Senior Director, ACRIN Diagnostic Imaging Trials
1818 Market Street
Suite 1600
Philadelphia, PA 19103-3604

APPENDIX 7: ACRIN PRELIMINARY PROTOCOL CONCEPT DEVELOPMENT

The Preliminary Protocol Concept Development form will be completed by the submitting individual in collaboration with the appropriate Disease Site Committee (DSC) Chair. The DSC Chair will forward the completed form to ACRIN Headquarters for consideration by the Steering Committee. Upon approval of the Steering Committee, the protocol trial team will be appointed to further develop the concept in the ACRIN Protocol Concept Submission document for NCI/CTEP review and approval.

This document is limited to no more than six (6) pages and each section should contain a brief description **in bullet format** (i.e. non-narrative), where it is applicable:

Preliminary Protocol Concept Development	
WORKING TITLE OF PROJECT:	<i>Title should include both the disease site and technologies of interest and along with the application.</i>
SUBMITTING INDIVIDUAL:	<p><i>Provide name of the individual submitting the concept, including the specialty, contact information, and the names of co-chairs or discipline chairs, if any.</i></p> <p><i>Name of the submitting member</i> <i>Specialty</i> <i>Address</i> <i>Phone</i> <i>Fax</i> <i>Email</i></p>
INTRODUCTION/ BACKGROUND	<i>Provide brief information/reasons for why this research is important, including a summary of clinical issues relevant to study and potential impact on, for example, overall survival, Quality of Life or proof of principle. How research strategy or future clinical practice will be altered by either positive or negative results. (250 words or less)</i>
SPECIFIC HYPOTHESIS:	<i>Briefly specify the hypotheses of the potential concept/protocol. Additionally, provide how the proposed concept addresses one or more of ACRIN key objectives.</i>
STUDY DESIGN:	<p><i>Briefly specify the design of the trial, including accrual plan for both clinical and correlative study designs, e.g. Health Outcomes/QOL, etc. (In bulleted format; a schema, if possible)</i></p> <p><i>Specify the type of image data submission requirements; types of imaging modalities to be utilized (e.g. CT, MRI, PET, etc.); who will perform image evaluation. (Refer to the Image Requirements Questionnaire to assist in completion of this section.)</i></p>
STUDY OBJECTIVE:	<i>Briefly indicate the primary two or three study objectives. What are the possible outcomes? (In bulleted format)</i>

ELIGIBILITY CRITERIA:	<i>Outline patient and/or disease characteristics required for participation. (In bulleted format)</i>
PRELIMINARY STATISTICAL DESIGN:	<i>Provide an estimate of sample size and expected analysis for this protocol concept.</i>
COMPETING PROTOCOLS:	<i>Provide a list of any competing/existing trials, similar to the protocol concept being developed, as well as any trials targeting the similar patient population that may hinder subject accrual. Include any industry, commercial and international trials. NCI (http://www.cancer.gov/clinicaltrials/) and American Cancer Society (http://clinicaltrials.cancer.org/) databases may be helpful in obtaining a list of competing trials</i>
KEY REFERENCES: (20 or less)	<i>In this section, provide any information and publications cited in the submission. It should be organized as any standard bibliography page (cite only the most important references).</i>
COMMENTS:	<i>Provide an estimation of financial incurrence to conduct the trial. Provide any additional information or comments that you would like the various committees to consider during the review process of the concept for approval.</i>

 Name of Person Completing Form

 Date

 Person Completing Form E-mail Address

 Phone Number

NOTE: Concepts must be submitted in electronic format by e-mail to the appropriate ACRIN parties:

- Appropriate Disease Site Committee (DSC),
- ACRIN Headquarters, or
- ACRIN Network Chair

With preliminary concept approval by the DSC, PI will present the concept to the ACRIN Steering Committee for SC approval to further development of the concept on the ACRIN Protocol Concept Submission document for NCI/CTEP review and approval.

Appendix 8: ACRIN PROTOCOL CONCEPT SUBMISSION (For submission to CTEP)

A Protocol Concept Submission document must be prepared upon approval from the ACRIN Steering Committee by the potential Principal Investigator (PI) using the *ACRIN Protocol Concept Submission Form* and forwarded to ACRIN Protocol Associate (PA) for submission to NCI/CTEP. The purpose of the ACRIN Protocol Concept Submission document is to gather detailed data concerning the developing study and to obtain approval from the appropriate sponsoring committees, organizations, and ACRIN Steering Committee in preparation for submission to NCI/CTEP for review and approval. The document is limited to minimum of five (5) pages and no more than nine (9) pages and will contain a brief description of the following **in bullet format** (i.e. non-narrative):

I. ADMINISTRATIVE INFORMATION	
DISEASE SITE/INDICATION:	<i>Provide the disease site area or the indication the potential study will target.</i>
SUBMITTING INDIVIDUAL:	<i>Provide name of the individual submitting the concept, including the specialty, contact information, and the names of co-chairs or discipline chairs, if any.</i> <i>Name of the submitting member</i> <i>Specialty</i> <i>Address</i> <i>Phone</i> <i>Fax</i> <i>Email</i> <i>Name(s) of Co-Chair(s)</i>
PROTOCOL CONCEPT TITLE:	<i>Insert the name/title of the protocol concept.</i>
STATISTICAL/DATA MANAGEMENT (From ACRIN BDMC):	<i>Insert the name of the statistician, and contact information. This individual must be a member of the ACRIN Biostatistical and Data Management Center.</i> <i>Name</i> <i>Address</i> <i>Phone</i> <i>Fax</i> <i>Email</i>

II. SCIENCE BACKGROUND	
WHY IS THIS STUDY IMPORTANT:	<ul style="list-style-type: none"> • <i>Describe why this is an important area for research.</i> • <i>Include a summary of clinical issues relevant to the trial setting and potential impact on important endpoints (for example, overall survival, quality of life, or proof of principle).</i> • <i>Describe how research strategy or future clinical practice would be altered by either positive or negative results.</i> • <i>For publications cited, include either NLM/Medline ID # or URL address to permit retrieval of the full text or abstract by reviewers (cite only most important references).</i>
SPECIFIC HYPOTHESIS:	<i>Briefly specify the hypotheses of the potential concept/protocol.</i>
STUDY DESIGN:	<p><i>Briefly specify the design of the trial, including both clinical and correlative study designs.</i></p> <p><i>Specify the basic imaging approach; types of imaging modalities to be utilized (e.g. CT, MRI, PET, etc.); and the availability of technology.</i></p>
RATIONALE:	<i>Briefly provide a rationale for the selected approach and study design of the concept/protocol.</i>
SUPPORTING PRELIMINARY DATA:	<p><i>Describe or provide justification for conducting the study.</i></p> <ul style="list-style-type: none"> • <i>Provide multi-center clinical data, including any of your own preliminary data for any correlative science studies integral to the trial.</i> • <i>For publications cited of results of similar studies or pilot data, include either NLM/Medline ID # or URL address to permit retrieval of the full text or abstract by reviewers (cite only the most important references).</i>
STUDY OBJECTIVE:	<i>Briefly indicate the primary objective (one main objective) and any other secondary objectives.</i>
ELIGIBILITY CRITERIA:	<p><i>Outline patient and/or disease characteristics required for participation.</i></p> <p><i>Provide rationales for selecting or excluding particular population.</i></p>

SCHEMA:	<p><i>Provide an outline/diagram of arms/regimen of the intervention plan of the study: an overview.</i></p> <p>SCHEMA:</p> <p style="text-align: center;"> S T R A T I F Y R A N D O M I Z E o r R E G I S T E R </p>
PRELIMINARY STATISTICAL DESIGN:	<p><i>Describe one primary and any secondary endpoints, any stratification to be used in the randomization, proposed sample size with power justification, analysis plan for formal interim analysis, projected monthly accrual rate, and information to support the projected accrual rate.</i></p>
SOURCE OF AGENTS:	<p><i>If applicable:</i></p> <ul style="list-style-type: none"> • <i>List the name of the sponsor or sub-specialty organization</i> • <i>Provide who will distribute non-IND and commercial agents</i> • <i>If IND agent, provide IND and NSC numbers and name of the IND holder</i>
FEASIBILITY:	<p><i>As appropriate, discuss:</i></p> <ul style="list-style-type: none"> • <i>The size of eligible population</i> • <i>Special equipment</i> • <i>Educational requirements of investigators</i> • <i>Anticipated acceptance of trial by patients and referring physicians</i> • <i>Competition with other large trials for similar patient population</i> • <i>Experience with accrual to similar trials</i>
iii. CORRELATIVE STUDY SECTION (IF APPLICABLE)	
CORRELATIVE STUDY DESIGN:	<p><i>Describe the rationale, the design, and preliminary data of any correlative study integral to the clinical study.</i></p> <p><i>For these sub-studies, include rationale, study design, specific hypothesis, and statistical design.</i></p> <p><i>Provide any funding source that will support the sub-studies.</i></p>

SPECIFIC HYPOTHESES:	<i>Briefly provide the hypotheses of the correlative study or studies.</i>
STATISTICAL DESIGN:	<i>For each correlative/sub-study, provide statistical design for:</i> <ul style="list-style-type: none"> • <i>Endpoints</i> • <i>Sample size</i> • <i>Monthly accrual rate</i>
KEY REFERENCES: (20 or less)	<i>In this section, provide any information and publications cited in the submission. It should be organized as any standard bibliography page. (Cite only the most important references.)</i>
COMMENTS:	<i>Provide any additional information or comments that you would like the various committees to consider during the review process of the concept for approval.</i>

 Printed Name of Person Completing Form

 Phone Number

 Email Address of Person Completing Form

 Date

Appendix 9: ACRIN CONFERENCE CALLS

Because ACRIN is a virtual network, many important decisions are made on conference calls. As an ACRIN PI, you are responsible for leading these calls. Staff at ACRIN Headquarters will help you develop call agendas. ACRIN staff will also take minutes and distribute reminders, minutes, and agendas.

During the concept and protocol development process, conference 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 process of the study.

During pre-activation and activation, the calls usually expand to involve site principal investigators and research associates 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.