



**ACRIN 4701 RESCUE**  
**RESCUE: Randomized Evaluation of Patients with Stable Angina**  
**Comparing Utilization of Diagnostic Examinations**

**SUMMARY OF CHANGES**

May 4, 2011

Amendment # 1

---

**Amendment 1 to the ACRIN 4701 RESCUE protocol reflects changes to trial procedures predominantly driven by multiple site types and their ability to provide protected health information to ACRIN for medical record collection; the amendment opens the procedures to allow US Veterans Affairs institutions to follow their routine practices for collecting and providing medical records for research. The protocol was previous written to allow only ACRIN-coordinated medical record requests/collection.**

**In addition to protocol changes for grammar, style, and clarify, the following highlights revisions: 1) add “pacemaker” among the Exclusion Criteria; 2) add “or TID with ECG changes of ischemia” among the diagnoses leading to ICA in the SPECT MPI group; 3) specify that the quality-of-life assessment for the trial will be conducted at US-sites only (foreign sites are exempt); 4) add lifestyle questions at baseline and 12-month follow up; 5) allow for collection of historical cardiac and hypertensive health information at baseline; 6) explain the expectations for/expand the timeline for ECG collection/performance at baseline and for medical record collection; 7) clarify that the Informed Consent Form Template (Appendix I) will need to be revised to accommodate site-specific procedures for medical record collection and QoL tool administration, reduce the amount of content and the reading grade level, ensure all study procedures are included and updated per amendment revisions, and explain the intended use of the authorization document to be signed by the participant when ACRIN is coordinating medical record collection; 8) clarify and simplify the Authorization for Release/Disclose Medical Records Template (Appendix II); and 9) ensure the Endpoint-Related Definitions (Appendix IV) match the definitions to be used by the adjudication committee.**

**Cover Page**

Dr. Tao Liu's email address has been corrected.

Amendment 1 and version date May 4, 2011, have been added.

**Table of Contents**

Page numbers were adjusted to match the current version.

**Schema, Page 3**

The trial Schema has been updated to include “or TID with ECG changes of ischemia” among the findings with SPECT MPI that will lead to diagnostic ICA.

The acronym definitions have been added to the footnote.

**Eligibility, Page 4**

“Pacemaker” and the unit measure for BMI, “kg/m<sup>2</sup>”, have been added to the bulleted list of exclusion criteria.

**Section 2.1, Standard Evaluation of Patients with Stable Chest Pain, Page 6**

2<sup>nd</sup> paragraph, new-final sentence: Has been added to describe that TID accompanied by ECG changes should lead to ICA.

**Section 3.0, Study Objectives/Specific Aims, Page 10**

1<sup>st</sup> sentence: "Appendix IV" has been corrected to "Appendix III".

**Section 4.0, Study Overview, Pages 11–14**

Pages 11–12: The Study Overview description has been revised to include "or TID with ECG changes of ischemia" among the findings with SPECT MPI that will lead to diagnostic ICA (see 2<sup>nd</sup> paragraph) and to describe that the quality-of-life questionnaires will be completed only by US sites and to introduce the lifestyle questionnaire (see now-5<sup>th</sup> paragraph).

The order of paragraphs has been revised to present a more linear description of the trial.

Page 13: The trial Schema (Figure 1) and Medical Chart Abstraction Flow Chart (Figure 2) have been updated to include "or TID with ECG changes of ischemia" among the findings with SPECT MPI that will lead to diagnostic ICA.

The acronym definitions have been added to the footnote.

**Section 5.2, Exclusion Criteria, Page 16**

New-Section 5.2.11: Has been added to exclude patients with pacemakers. Subsequent sections have been renumbered.

Now-Section 5.2.17: The unit measure for BMI, "kg/m<sup>2</sup>", has been added.

**Section 5.3, Recruitment and Screening, Page 16**

1<sup>st</sup> paragraph, new-2<sup>nd</sup> sentence: Has been added to confirm that "*Patients presenting to the emergency department may be eligible for the trial as long as acute coronary syndrome is ruled out and all other eligibility criteria are met for trial participation.*"

**Section 5.4, Inclusion of Women and Minorities, Page 17**

"Table 3" has been added to the header for the Gender and Minority Accrual Estimates table.

**Section 6.1, Institution Requirements, Pages 17–19**

Section 6.1: 1<sup>st</sup> paragraph, 1<sup>st</sup> sentence: Reference to the General Qualifying Application (GQA) has been deleted as only the Protocol Specific Application (PSA) will be required for site selection to this trial.

1<sup>st</sup> paragraph, new-2<sup>nd</sup> sentence: Has been added to state that the PSA will be reviewed by the ACRIN Institutional Participant Committee.

2<sup>nd</sup> paragraph, 1<sup>st</sup> sentence: Reference to the participation of VA medical facilities has been added.

Section 6.1.1: 1<sup>st</sup> paragraph, 2<sup>nd</sup> sentence has been deleted as technical details will be collected in the PSA document.

Section 6.1.2: 1<sup>st</sup> paragraph, 1<sup>st</sup> sentence: Language referencing Tufts Medical Center and the SPECT MPI core lab has been revised.

1<sup>st</sup> paragraph, 2<sup>nd</sup> sentence: "Stress" has been revised to "SPECT".

1<sup>st</sup> paragraph, former-3<sup>rd</sup> sentence: Has been deleted as technical details will be collected in the PSA document.

Section 6.1.3: 1<sup>st</sup> paragraph, 1<sup>st</sup> sentence: "showing CAD" has been deleted.

1<sup>st</sup> paragraph, 3<sup>rd</sup> sentence: "Table 3" has been updated to "Table 4".

Now-Table 4: Header has been updated and the SPECT MPI details have been revised.

Below Table 4: 1<sup>st</sup> paragraph: Contact information for Cynthia Price at ACRIN core lab for the CCTA component has replaced Dena Flamini.

2<sup>nd</sup> paragraph: Email information for Rebecca Scaven has been updated to “@acr.org”.

3<sup>rd</sup> paragraph: “at Massachusetts General Hospital” has been added.

4<sup>th</sup> paragraph: “at Tufts Medical Center” has been added.

### **Section 6.2, Regulatory Requirements, Page 20**

1<sup>st</sup> paragraph, new-4<sup>th</sup> through 6<sup>th</sup> sentences: Have been added to explain the intended use of the Authorization to Release/Disclose Medical Records Template (Appendix II) and the use of this document among institutions coordinating their own medical record collection.

2<sup>nd</sup> paragraph, 2<sup>nd</sup> sentence: “and authorization document (as appropriate)” has been added so sites know to submit their local IRB-approved authorization document to ACRIN as appropriate.

### **Section 6.3.3, Safety Monitoring and Independent Clinical Event Adjudication Committee, Page 21**

2<sup>nd</sup> paragraph, 3<sup>rd</sup> sentence: Has been revised to clarify the adjudication process—a minimum of three adjudications “will be available” to review and adjudicate medical records for all “MACE and revascularization while blinded to study arm”.

### **Section 8.0, Study Procedures, Pages 24–25**

1<sup>st</sup> paragraph, 1<sup>st</sup> sentence has been revised to present an outline of the initial study visit and follow-up contacts. Details have been added in relation to the baseline quality-of-life (QoL) questionnaires (US sites only) and the addition of the lifestyle questionnaire. Reference to mailing the QoL questionnaires has been deleted as some sites administering the questionnaire may opt to do so while the patient is visiting the facility.

2<sup>nd</sup> paragraph, new-1<sup>st</sup> sentence: Has been added to specify “*Medical record collection will be required for adjudication for participants with a MACE or revascularization.*”

2<sup>nd</sup> paragraph, now-2<sup>nd</sup> and 3<sup>rd</sup> sentences: Have been revised to clarify abstraction versus adjudication and to allow for site RAs to coordinate medical record collection.

3<sup>rd</sup> paragraph, new-3<sup>rd</sup> sentence: Has been added to introduce Table 5, which outlines the distinctions in procedures between non-VA US sites, US VA sites, and foreign sites participating in the trial.

### **Section 8.1, Phase I: Baseline Assessment, Pages 25–26**

Section 8.1.1.2: 1<sup>st</sup> bullet introduces review of past medical history at baseline to determine cardiac or hypertensive tendencies.

Section 8.1.1.3: “NOTE” has been added to explain that “*VA and foreign sites may be exempt from submitting PHI for study purposes, depending on their local policy. Other sites may request exemption and will be considered on a site-by-site basis.*” Additional details are available in Sections 8.2 and 8.3.

Section 8.1.1.4: Has been revised to expand on the ECG at baseline—originals are preferred, but color copies are sufficient; electronic submission or color photocopies by mail are sufficient. ECGs completed within “30 days prior to diagnostic imaging” for the trial will be acceptable for submission to ACRIN. Otherwise, the baseline ECG should be completed at the time of diagnostic imaging.

Section 8.1.1.6: Has been revised to specify that the QoL questionnaires will be completed at US sites only and that foreign sites are exempt.

New-Section 8.1.1.7: Has been added to introduce the administration of the lifestyle questions by research staff for participant self-report at baseline.

### **Section 8.1.3, Phase 3a: Group A—CCTA, Page 26**

Section 8.1.3.1: A period has been replaced with a semicolon for consistency.

NOTE, new-final sentence: Has been added to specify that, in the event that CCTA rescanning is necessary in a participant, data from the initial and any second imaging will be collected.

**Section 8.1.4, Phase 3B: Group B—SPECT MPI/ICA, Page 26**

NOTE, 2<sup>nd</sup> sentence: Has been revised to read as follows—*“Should the examination be un-evaluative, the SPECT MPI will be considered positive for study analysis. The research team recommends and encourages reviewing rest and stress images post-acquisition for quality before the participant is released from the scanner and rescanned, if necessary. For STRESS TI-201 imaging: If motion compromises a study, the benefit of rescanning is uncertain; the treating physician should determine further diagnostic assessment. Data from both imaging studies will be collected.”*

**Section 8.1.5, Phase 4: Post-CCTA or SPECT MPI/ICA, Treatment as Appropriate, Pages 26–27**

Section 8.1.5.1: 2<sup>nd</sup> and 5<sup>th</sup> bullets: “or TID with ECG changes of ischemia” has been added among the findings with SPECT MPI that will lead to diagnostic ICA.

Section 8.1.5.2: Final sentence has been revised to clarify that adherence to OMT will be documented based on participant follow up and details abstracted from the participant’s medical record.

**Section 8.2, Follow Up: Telephone Contacts, Quality of Life Mailings, and Medical Records Abstraction, Pages 28–30**

Header has been updated to write out “Quality of Life”.

Section 8.2.1: 2<sup>nd</sup> paragraph, item #2: “or TID with ECG changes of ischemia” has been added among the findings with SPECT MPI that will lead to diagnostic ICA.

4<sup>th</sup> paragraph (below Follow Up Time Points table), 3<sup>rd</sup> sentence: Has been revised to define a follow up time point as complete once contact is made or vital status has been verified.

Section 8.2.1.1.2: “stroke” has been added to the triggers for abstraction along with MACE and revascularization.

New-Section 8.2.1.1.6: Has been added to introduce the lifestyle questions at 12-month follow-up only.

Former-Section 8.2.1.1.6: Has been deleted as AE-related will not be asked at 6-month follow-up intervals (only at the time of CCTA).

Section 8.2.1.3: Has been revised to confirm that follow-up forms should be completed after the fourth attempt to reach the participant, or with confirmation of vital status, at each follow-up time point.

Section 8.2.1.4: 1<sup>st</sup> sentence has been revised to allow follow-up forms to contain the complete span of time since last contact with the participant was made—so if contact is not made until 12 months, a single form will collect details from enrollment through 12 months. Abstraction will delineate into 6-month time frames for the trial analysis.

New-2<sup>nd</sup> sentence: Has been added to clarify that the lifestyle questions should only be completed if contact is made at the 12-month follow-up time point.

Section 8.2.1.5: 1<sup>st</sup> sentence has been revised to read “medical record collection” instead of “medical chart abstraction” as the list provided covers all instances triggering medical record collection, including adjudication; “stroke” has been added.

New-2<sup>nd</sup> and 3<sup>rd</sup> sentences have been added to allow local institutional policy to determine whether ACRIN or site research staff will coordinate medical record collection and to introduce Table 5, which provides an overview of the procedures by institution type.

New-Table 5 has been added to provide an overview of adjudication, abstraction, and QoL procedures by site type—non-VA US sites, US VA sites, and foreign sites.

**Section 8.2.2, QoL Questionnaires (At 12-Month Follow Up for Subset of Participants Only),**

**Pages 30–31**

Header has been updated to “QoL” Questionnaires since not all sites will be mailing the questionnaires for participant completion.

Section 8.2.2 has been revised to allow for local policy to determine whether the ACRIN Outcomes and Economics Unit (AOEU) or site research staff will coordinate completion of the QoL questionnaires at 12-month follow-up. Sites not using AOEU to coordinate this trial component will be responsible for follow up to encourage participants to complete the questionnaires and are welcome to coordinate the completion of the forms by mail (preferred), phone, or in-person.

Section 8.2.2 includes language exempting foreign sites from the QoL component of the trial.

**Section 8.3, Medical Record Abstraction, Pages 31–32**

Section 8.3.1.1: 1<sup>st</sup> sentence has been revised to remove reference to incidental findings as a trigger for medical record abstraction.

Section 8.3.1.2: Item #1: “stroke” has been added.

Item #4: Submission of ECGs with medical records has been clarified as follows—“(color photocopies are sufficient and may be submitted electronically or by mail)”.

Section 8.3.1.3: Former-2<sup>nd</sup> sentence has been deleted to allow sites to coordinate medical record collection instead of centralizing the process through ACRIN.

Section 8.3.2.3: 1<sup>st</sup> sentence has been revised to confirm abstraction will be performed directly onto electronic forms for the trial.

Former-Section 8.3.2.4: Has been deleted as the electronic forms submission process does not necessitate data collection to laptops or back-up to a centralized computer.

Now-Section 8.3.2.4: Foreign sites are no longer expected to translate their medical records but instead to perform their own abstraction of the medical record data pertaining to the primary aim of the trial, and these sites are exempt from the QoL component of the trial.

**Section 8.5, Study Procedures Table: Site Activities, Pages 33–34**

10<sup>th</sup> Row, 1<sup>st</sup> Column: Has been revised to explain ECG at baseline can be performed wutgub 30 days prior to diagnostic imaging or at the time of diagnostic imaging.

10<sup>th</sup> Row, 6<sup>th</sup> Column: Includes a parenthetical allowing for ECG submission with medical record collection only “(If Performed During Follow-Up Cardiac Visits)”.

12<sup>th</sup> Row, 1<sup>st</sup> Column: Has been revised to read—“Administer Questionnaires (QoL at US Sites Only)”.

23<sup>rd</sup> Row, 1<sup>st</sup> Column: “Complete” has been added.

24<sup>th</sup> Row, 6<sup>th</sup> Column: The “X” has been deleted for AE assessment at follow up time points. AEs will be assessed at the time of the CCTA.

Footnote \*: New-2<sup>nd</sup> sentence has been added revised to explain that 2-week and 2-month telephone contact for participants with positive diagnostic findings will be limited to questions related to MACE, stroke, and revascularization.

The final sentence has been added to specify that lifestyle questions will be asked during the 12-month follow-up contact time point.

Footnote †: Has been revised to describe “medical record collection for abstraction” instead of “medical chart abstraction” and that self-report of “stroke” is among the triggers for record collection.

**Section 8.6, Study Procedures Table: Participant Activities, Page 34**

New-12<sup>th</sup> Row: “Stroke” has been added as participants will be asked about stroke events at all applicable follow-up time points.

19<sup>th</sup> Row, 1<sup>st</sup> Column: Has been revised to read “SF-36 and Seattle Angina QoL Tools” instead of having the two tools on separate lines.

New-20<sup>th</sup> Row: “Lifestyle Questions” has been added for completion at baseline and 12-month follow up.

Footnote §: Has been updated to allow for “completion of” questionnaires to be coordinated by “the site or” the ACRIN Outcomes and Economics Unit. A sentence has been added exempting foreign sites from administering the QoL tools.

**Section 9.1.3, CCTA Reading for Stenosis, Page 36**

4<sup>th</sup> sentence: Has been revised to describe a central read instead of an “over read” to “assess” the quality of data from local CCTA interpretations.

5<sup>th</sup> sentence: Has been revised to clarify that the revised jeopardy score will be created using modified Duke Prognostic Index and other myocardial jeopardy scores “based on the local read”.

**Section 9.1.3.1, Coronary Artery Stenosis, Page 37**

Final sentence, contact information: “at Massachusetts General Hospital” has been added.

**Section 9.2, SPECT MPI Recommendations, Pages 37–39**

Section 9.2: 1<sup>st</sup> sentence has been revised to read—“The SPECT MPI core lab at Tufts Medical Center, ...”.

2<sup>nd</sup> sentence: “at Tufts Medical Center” has been added.

Former-4<sup>th</sup> sentence: Has been deleted as a separate survey is not being requested of potential sites.

Now-4<sup>th</sup> sentence: Has been revised to read—“The ACRIN 4701 RESCUE SPECT MPI Imaging Acquisition Recommendations form is available online at ...”.

Section 9.2.1: 1<sup>st</sup> sentence has been revised to read—“...to ensure optimal imaging techniques are performed.”

Section 9.2.2: 1<sup>st</sup> paragraph, former-1<sup>st</sup> sentence has been deleted as sample reports are not required from potential sites.

1<sup>st</sup> paragraph, now-1<sup>st</sup> sentence: “for SPECT MPI” has been added for clarity.

3<sup>rd</sup> paragraph: Has been extensively revised to clarify what is required from each site for ACRIN core lab review of SPECT MPI and how feedback will be provided to the sites from the ACRIN core lab and the SPECT MPI core lab at Tufts Medical Center.

5<sup>th</sup> paragraph: “at Tufts Medical Center” has been added for clarity.

**Section 9.3, Quality Control for CCTA and SPECT MPI Images, Pages 38–39**

Section 9.3.1.3: 2<sup>nd</sup> sentence has been revised to explain the process and delivery of feedback for radiation exposure oversight—“*For the study-related CCTA imaging, sites will be contacted should radiation exposure exceed a mean of 15 mSv, to be assessed monthly by site and sites over the mean of 15 mSv base don the last 5 cases will be contacted by the trial PIs.*”

Section 9.3.2.1: Has been revised to explain “Expert Central Reads” instead of an over-read process. Central reads will be blinded to local interpretation and involve only 10% of participant CCTA and SPECT MPI cases. The aim of the central read is to assess quality of local reads.

Former-Section 9.2.3.2: Has been deleted, as protocol compliance will be routinely assessed per ACRIN standard procedures, monitoring, auditing, quality assurance, and BDMC oversight.

**Section 9.4, Image Submission, Page 39**

2<sup>nd</sup> paragraph, final sentence: The email address for Triad Support has been updated to [Triad-Support@acr.org](mailto:Triad-Support@acr.org).

**Section 10.2, Definitions of Serious Adverse Events, Page 40**

1<sup>st</sup> paragraph, new-final bullet: *“Requires intervention to prevent any of the above, per the investigator/sponsor”* has been added.

New-2<sup>nd</sup> paragraph, defining Life-Threatening Adverse Event: Has been added.

**Section 10.7, Recording of Adverse Events, Page 43**

4<sup>th</sup> paragraph, former-1<sup>st</sup> sentence: Has been deleted as it references assessment of AEs at every participant contact, but only CCTA-related AEs will be collected at the time of the imaging study.

**Section 15.0, Statistical Considerations, Pages 48–53**

1<sup>st</sup> paragraph, 3<sup>rd</sup> sentence: “Appendix III” has been corrected to “Appendix IV”.

1<sup>st</sup> paragraph, new-5<sup>th</sup> sentence: Has been added to introduce the lifestyle questions, administered at baseline and 12-month follow-up time points.

Section 15.1.1: 2<sup>nd</sup> paragraph, 4<sup>th</sup> sentence: Has been split into two sentences. The now-5<sup>th</sup> sentence has been revised to describe that all reports will be reviewed by the outcomes adjudication committee.

Section 15.2.2.1: 2<sup>nd</sup> paragraph, 5<sup>th</sup> sentence has been revised to confirm abstraction will be performed directly onto electronic forms for the trial.

2<sup>nd</sup> paragraph, former-final sentence: Has been deleted as the electronic forms submission process does not necessitate data collection to laptops or back-up to a centralized computer.

Section 15.2.3.1: 4<sup>th</sup> paragraph, 1<sup>st</sup> sentence: “sites or” has been added to allow for the administration of the QoL questionnaires by the site’s research staff instead of the ACRIN Outcomes and Economics Unity.

Section 15.2.3.2: 1<sup>st</sup> paragraph, 1<sup>st</sup> sentence: “each participant at each timepoint” has been corrected to “selected participants” as not all participants will complete the 12-month follow-up QoL questionnaires.

**Appendix I, Informed Consent Form Template, Pages 62–75**

**General:** The Informed Consent Form Template has been revised to reduce redundancy, improve language/decrease reading grade level, and ensure all trial components are included in the template for sites to create their appropriate site-specific versions for local IRB submission and approval.

The Title has been revised to introduce bolding of the capital letters that spell out “RESCUE” and to add “RESCUE” to the title line.

A “Disclaimer” has been added to inform the participant that the “RESCUE” acronym in no ways indicated any health benefit related to the decision to participate in the trial.

A description has been added to the beginning of the protocol to describe that the template will need to be revised as appropriate for site-specific practices in release of protected health information (PHI) and medical record collection, and to remind foreign sites that they are exempt from the QoL component of the trial:

*“<<Depending on institutional practices related to protected health information (PHI) and the release of PHI for trial conduct (that is, medical record collection), sections of the trial description may need to be deleted, such as reference to collecting the patient’s Social Security Number and the authorization document for medical records collection. Content related to the quality-of-life questionnaires at baseline and at 12-month follow up will need to be removed from all foreign-site*

*questionnaires. If you need assistance in revising the ICF Template for your institution, contact the ACRIN 4701 RESCUE trial monitor.>>*

**Under “Why Is This Study Being Done?”:** 1<sup>st</sup> paragraph, 2<sup>nd</sup> sentence has been deleted as it is repetitive (trial design is described again later in the section). The former-2<sup>nd</sup> paragraph has been moved up to add to the 1<sup>st</sup> paragraph.

Now-2<sup>nd</sup> paragraph, 1<sup>st</sup> sentence: “while” has been added.

Now-3<sup>rd</sup> paragraph, 1<sup>st</sup> sentence: “study-related imaging” has been replaced with “experimental group uses imaging” for clarity.

Now-4<sup>th</sup> paragraph, 2<sup>nd</sup> sentence: “1)” and “2)” have been added to highlight the treatment pathways for patients diagnosed with a heart condition.

New-5<sup>th</sup> and 6<sup>th</sup> paragraphs: Have been added and re-write the description of why the study is being done to present the detail as a bulleted list and describe that previous research leading to the treatment paradigm for this trial, as follows—

*“The purpose of this research is to:*

- *Compare patient outcomes after diagnosis with either coronary CT or nuclear medicine cardiac stress test results;*
- *Determine the appropriate use of medication and lifestyle change in clinical care; and*
- *Compare costs associated with these approaches to care.*

*The study doctors are hoping to be able to correctly diagnose heart disease and reduce the need for diagnostic tests and treatments while safely treating the condition. Previous research has shown that treatment with medicine and lifestyle change is safe and may reduce the need for additional diagnostic testing or surgery.”*

**Under “About Diagnostic Invasive Coronary Angiography (Group B),** 1<sup>st</sup> paragraph: The first four sentences have been revised to read—*“You may need to have an additional diagnostic test called invasive coronary angiography. It will depend on the results of your nuclear medicine cardiac stress test. This test is part of standard care. A catheter—a small tube—is woven up from a blood vessel, usually in the upper thigh, through the body, and into the arteries that run outside of the heart.”*

**Under “How Many People Will Take Part in the Study?”,** 2<sup>nd</sup> sentence: Has been deleted to reduce redundancy because randomization is described later in the template.

**Under “How Long Will I Be in the Study?”,** 1<sup>st</sup> paragraph, 2<sup>nd</sup> sentence: Has been rewritten for clarity to read—*“A member of the study staff will contact you or someone you designate (a proxy) by phone about your heart and other health up to six times, and you may be asked to complete questionnaires for the study.”*

1<sup>st</sup> paragraph, former-3<sup>rd</sup> sentence: Has been deleted to reduce redundancy.

**Under “What Am I Being Asked to Do in the Study?”,** former-1<sup>st</sup> paragraph: Has been deleted because randomization is described later in the section.

2<sup>nd</sup> paragraph, former-2<sup>nd</sup> through 4<sup>th</sup> sentences: Have been deleted and replaced with a simplified description of the number of times a participant may be contacted by phone for the trial, as follows—*“You will be contacted by telephone up to six times, depending on your diagnosis and when you join the trial.”*

**Above “When You Join the Trial ...”:** A description has been added above the template section describing the study procedures to inform sites to revise the template according to their site-specific trial conduct related to the release of protected health information (PHI), medical record collection, and administration of QoL questionnaires (US sites only), as follows—*“<<Depending on institutional practices related to protected health information (PHI) and the release of PHI for trial conduct, sections of the trial description may need to be deleted, such as reference to collecting the patient’s Social Security Number*

*and the authorization document for medical records collection. Content related to the quality-of-life questionnaires at baseline and follow up will need to be removed from all foreign-site questionnaires.>>*

**Under “When You Join the Trial ...”, new-1<sup>st</sup> paragraph:** Has been added to describe the tests and procedures needed to determine the participant’s eligibility for the trial, as follows—

*“The following tests and procedures will be performed to determine if you qualify to take part in this study:*

- *Review of your medical history including your history of heart-related illnesses, trends in heart health (such as your blood pressure), and recent blood test results.*
- *Blood collection to check your kidney health, if not checked within the past 28 days (this may mean a vial of blood has to be drawn for the test).*
- *Pregnancy test if you are a woman who may be able to become pregnant. The result of the pregnancy test must show that you are not pregnant for you to qualify to participate in the study.*
- *You will be asked to sign a separate authorization to release some or all of your medical records for review and collection in this study.”*

2<sup>nd</sup> paragraph, new-1<sup>st</sup> sentence: Has been added and the bulleted list has been revised for parallel construct.

2<sup>nd</sup> paragraph, 2<sup>nd</sup> bullet: The ECG description has been revised to inform that participants may need to have an ECG at the time of diagnostic imaging if one is not available for submission to ACRIN from within the 30 days prior to diagnostic imaging.

2<sup>nd</sup> paragraph, 3<sup>rd</sup> bullet: Has been revised to include a third questionnaire at baseline (lifestyle questions), which should take about 5 minutes for the participant to complete.

**Under “Diagnosis: Randomized to One of Two Groups ...”:** Header has been revised.

1<sup>st</sup> paragraph: The description of the two study groups has been revised for clarity and to reduce reading grade level.

2<sup>nd</sup> paragraph: Has been simplified to describe the trial randomization and 50/50 chance of being assigned to either of the study groups.

**Under “Treatment”:** 2<sup>nd</sup> sentence, “disease” has been revised to “condition”.

**Under “Follow Up: Phone Contact, Questionnaires, and Medical Record Review”:**

Descriptions in the first four paragraphs for the follow-up procedures have been re-written to simplify and clarify the distinctions in procedures while updating the content for site-coordinated administration of the QoL questionnaires, as follows—

*“If you are diagnosed with heart disease during the study, a member of the study staff will contact you by telephone a minimum of four times (at 2 weeks, 2 months, 6 months, and 12 months after you join the study). You may also be contacted at 18 and 24 months after you join the study.*

*If you are not diagnosed with heart disease during the study, a member of the study staff will contact you by telephone, a minimum of two times (at 6 months and 12 months after you join the study). You may also be contacted at 18 and 24 months after you join the study, for a possible total of 6 times that someone may contact you for the study.*

*You will be asked to provide information about your heart-related and other health treatment and who has been treating you and where. With your permission and signed authorization of release of medical records form which you signed at the beginning of the study, the study staff will contact your treating doctors to request medical records for any treatment you may have received.*

*You also will be asked about the time and effort you have put into taking care of your heart (driving distances, amount of time). You may want to keep track of these details to make it easier for you to remember.*

*At 12 months after you join the trial, you may be asked to complete the same two questionnaires asking about your health and quality of life that you filled out at the beginning of the trial. People who receive the questionnaires will be randomly chosen. If you receive them, you will need to fill these out again and return them to research staff or in the envelope provided. These two questionnaires will take a total of about 20 minutes to complete.”*

**New—Under “Medical Records Collection”:** This new section describes the “authorization to disclose/release medical records” and procedures for withdrawing permission to collect medical record information for the trial, as follows—

*“At the baseline assessment, your study doctor will ask you to sign a separate document called ‘authorization to disclose/release medical records’ to obtain some or all of your medical records from your doctor. A separate authorization is needed for the research doctors to collect and review the information regarding your heart health and treatments you have received. Your medical records will be collected and sent to ACRIN. The study staff will remove information that can identify you from your medical records. Your medical records will continue to be collected until the end of the study unless you withdraw your authorization in writing, as described in the separate authorization to release medical records.”*

**Under “Study Chart”:**

2<sup>nd</sup> row, 2<sup>nd</sup> column, for Phase 1:

- Blood collection for testing kidney health has been added (if not checked within 28 days prior to enrollment);
- ECG description has been updated to reflect that it will only need to be performed if ECG results are not available from within the 30 days prior to diagnostic imaging;
- Three questionnaires will now need to be completed during Phase 1 (including the lifestyle questions) and will take a total of about 25 minutes.

8<sup>th</sup> row, 2<sup>nd</sup> column, for Telephone Contact: 1<sup>st</sup> bullet, “additional” has been deleted.

9<sup>th</sup> row, 1<sup>st</sup> column, for Questionnaires: Time point description has been revised to delete “By Mail” and to specify that the QoL tools will be administered to “US” participants only.

9<sup>th</sup> row, 2<sup>nd</sup> column, for Questionnaires: New-3<sup>rd</sup> sentence has been added to explain—“Some participants may be asked to complete the questionnaires at their institution or by phone.”

**Under “Risks Associated With Nuclear Medicine Stress Tests (With Pharmacologic Stress Agent)”:** Under “Rare”, 2<sup>nd</sup> bullet, “(temporary)” has been added to define “transient”.

**Under “What Are the Costs of Taking Part in This Study?”:**

1<sup>st</sup> sentence, “responsible” has been revised to “billed”.

Final sentence, “charged” has been revised to “billed”.

#### **Appendix II, Authorization to Release/Disclose Medical Records Template, Pages 76–77**

This template is designed for the participant to sign at the time of consent for use by ACRIN when ACRIN is coordinating medical record procurement from institutions. Revisions are to shorten and clarify the intended use of the template, who will receive a copy of the original, and withdrawal procedures. Reference to claim forms and billing records has been deleted as these documents will not be requested.

#### **Appendix IV, Endpoint-Related Definitions, Page 79**

The definitions for the primary endpoint analysis—for MACE (cardiac-related death or AMI) and revascularization—have been updated to provide an overview of and the more accurately reflect the definitions being used by the adjudication committee for the RESCUE trial, including those defined by the *Universal Definition of Myocardial Infarction* typing categorizations/classifications.