Ancillary Studies Charter

Version 2.0

May 18, 2016

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1.0 Guiding Principles for Ancillary Study Development and Approval

Investigators both within and outside the REPRIEVE trial will be encouraged to develop ancillary and databank studies. Ancillary studies are investigations that are not part of the REPRIEVE main trial, but that propose questions and test hypotheses that are relevant to and further the goals and purposes of REPRIEVE. An ancillary study may require the collection of additional data, e.g. clinical, imaging, biomarkers, genetic and outcome data during the course of the trial. Databank studies may use the findings obtained in the trial that are reformatted or analyzed in a novel fashion. For example, the presence of certain already ascertained patient characteristics and clinical outcomes may be analyzed in an effort to improve risk stratification. It is recognized that well designed ancillary studies, consistent with the goals of REPRIEVE, can leverage the study's resources to provide critical answers to highly relevant questions for the field. In contrast, ancillary studies that may impede the primary or secondary goals of REPRIEVE, either by burdening patients, study investigators or study sites, jeopardizing the collection of primary and secondary data, or investigating questions not relevant to the scientific goals of REPRIEVE, will not be recommended for approval. In addition, proposals that do not have adequate resources to perform the outlined ancillary studies will not be approved. It is further recognized that REPRIEVE will not be able to furnish significant resources to fund any ancillary study or team and that successful ancillary studies should be able to secure adequate funding through peer review, either through the ACTG, NIH or other funding sources (see Funding in Appendix 1).

This charter sets forth basic principles regarding ancillary studies to be requiring the collection of additional data that is not already collected within the REPRIEVE study. Toward the end of the study, proposals seeking to utilize already captured data and stored specimens not being analyzed in REPRIVE will be solicited, and this process is also outlined.

2.0 Summary of the Ancillary Study Review Process, Goals and Requirements for Studies Requiring Collection of Additional Specimens or Tests

The REPRIEVE Ancillary Study Committee (ASC) is charged with the review, and recommendation for approval of ancillary studies to the Executive Committee of REPRIEVE, for a final vote. An additional function of the ASC will be to make the EC aware of important new research opportunities, including those proposed by outside investigators for REPRIEVE. These

could include additional trials or investigations to be carried out during the current or future funding periods.

The Executive Committee (EC), including representatives from NHLBI and DAIDS, will hold the authority to approve any ancillary studies recommended for approval by the ASC. Voting members of the EC will be Drs. Grinspoon, Hoffmann, Douglas, Ribaudo, Currier, Allston-Smith andDesivgne-Nickens. In this process, the EC will take into account logistical and regulatory considerations, including but not limited to scientific merit, advancing the goals of REPRIEVE, feasibility, and potential for peer reviewed funding source.

A major purpose of REPRIEVE is to facilitate collaborations between Heart, Lung and Blood (HLB) and HIV experts. Multi-disciplinary scientific partnerships were indeed a key recommendation from the 2012 NHLBI AIDS Working Group. It is anticipated that ancillary study proposals for REPRIEVE may come from investigators within REPRIEVE, the ACTG, and/or investigators who are not affiliated with the trial. Ancillary studies focused on HIV-related cardiovascular disease will be prioritized. Moreover, collaborative proposals that include ACTG REPRIEVE investigators who are enrolling patients will also receive priority. Utilization of the imaging core is encouraged. There will be two pathways for ancillary studies to be forwarded to the ASC for review.

3.0 Investigator Teams

3.1 ACTG Investigator Teams

For ACTG investigative teams, initial concept sheet proposals will first be reviewed by the ACTG, and only those concept proposals approved by the ACTG ITSG will be reviewed by the REPRIEVE ASC. It is anticipated that the ACTG will collect concept proposals for review at specific time points early on in the course of REPRIEVE, such that multiple proposals can be reviewed simultaneously through the ACTG, and judged with respect to each other and available resources. In its review, the ACTG will recommend to the protocol investigative team if it feels that the costs of the proposal can be covered by ACTG funds, or if the investigative team will be recommended to apply simultaneously for outside funding sources, for example to the NIH, to support the proposed studies. A limited number of concept proposals judged meritorious by the ACTG ITSG committee, will be forwarded to the ASC for review and ultimately for vote by the EC. The ACTG ITSG includes members who are part of the REPRIEVE protocol team, to ensure that the ITSG discussions and decisions are fully informed. In addition to providing a list of recommended proposals, the ITSG will provide the REPRIEVE ASC a list of proposals not

recommended, in order that the REPRIEVE ASC can fairly judge and place into context all submitted proposals, including those from outside the ACTG.

3.2 Investigator Teams not Primarily Affiliated with the ACTG

For investigators not primarily affiliated with the ACTG, pursuing independent funding (e.g. NIH, industry), concept proposals should be submitted directly to the REPRIEVE ASC for review. Such proposals may include ACTG investigators in a collaborative role, to further the goals of REPRIEVE, as outlined above.

Concept proposals will be reviewed with respect to the criteria outlined below.

4.0 Submission of Concept Sheet and Criteria for ASC Review

Investigators wishing to pursue an ancillary study shall submit a 3 page concept sheet to the REPRIEVE ASC (see attached), or to the ACTG ITSG, depending on the nature of the proposed ancillary study and potential funding source, as outlined above. The format includes: Background, Specific Aims/hypotheses, Significance, Methodology, Feasibility and collaboration, Statistical analysis and power calculations, Proposed funding mechanism, Budget, and References (see attached template). The proposed budgets for ancillary studies should include projected costs associated with implementing and monitoring the study (See Funding, Appendix 1). Investigators are encouraged to contact the REPRIEVE DCC and ACTG to obtain realistic estimates for these projections. There is no additional funding in REPRIEVE to support ancillary studies, and thus all proposed studies must detail the sources and amounts of funding adequate to cover the proposed investigation. The following items will be of particular importance to the ASC in evaluating concept proposals:

1. Scientific Importance
2. Feasibility/Impact on Parent Trial
3. Proposed Funding Source/Adequacy of Proposed Budget
4. Potential for Successful External Peer Review
5. Multi-Disciplinary Collaboration
6. Site PI partnership

5.0 Ancillary Study Committee Review and Procedures for EC Approval (See attached flow chart)

6.0 Initial Evaluations of Concept Proposals

The ASC will evaluate the importance, scientific merit and the proposed approach for each concept. In addition, it will determine feasibility of the study and assure that it will not have an adverse effect on: 1) the conduct of the primary study, including unintentional unblinding, and issues of patient safety and comfort; 2) patient enrollment and retention; and 3) the human and financial resources required to conduct the primary study. The ASC will review whether any additional blood is needed to conduct the ancillary study, how this will be obtained, shipped and stored and whether this will affect the blood drawing and storage limits of the main REPRIEVE study. For proposals that come from investigators outside the ACTG, the ASC will also review the proposal with the ACTG leadership to insure that the proposal is consistent with the goals of the ACTG, and can be accomplished as a REPRIEVE substudy using the existing ACTG infrastructure and trial structure. The ASC will make recommendations about each proposed ancillary study to the Executive Committee which will then vote on the proposed ancillary study. In addition, concept proposals approved by the EC will be briefly reviewed by the DSMB Chair at this initial stage, before a decision is communicated to the proposing investigative team, to insure the concept proposal is consistent with the goals of REPRIEVE. It is possible that a concept proposal will be returned for revision before a final decision is made.

7.0 Development and Peer Review of Approved Concept Proposals

Proposals approved by the REPRIEVE EC and DSMB at the concept stage, will be sent back to the proposing investigative team for further development. During the period of detailed protocol development, the investigative team of an approved concept proposal will be required to consult with the REPRIEVE ASC and will be assigned a designated protocol committee liaison to maximize the opportunity of obtaining important information without posing risks to the conduct of the trial and to insure adequate funding is requested to cover the costs of the trial. The ASC will review the fully developed protocol prior to submission for external peer review, to insure that the proposed application and fully developed protocol, remains of high scientific merit and is consistent with the goals of REPRIEVE and continues to satisfy criteria outlined above, in terms of feasibility/ impact, detailed budget, collaborative nature of proposal. This review will include a formal statistical review to ensure studies are adequately powered and do not compromise blinding in any way. Fully developed ancillary study protocols that are approved

by the REPRIEVE ASC and EC, will be submitted to external peer review for funding consideration by the ancillary study proposal team. Protocols approved for submission for external peer review by REPRIEVE will receive a Letter of Support from REPRIEVE to attach to the peer review application. For protocols developed within the ACTG, the ACTG Protocol review process will constitute peer review if external funds are not needed and the ACTG can cover the cost of the proposed ancillary study. If external funds beyond ACTG resources are needed, external peer review to obtain these funds, will be also necessary.

8.0 Final Approval of Ancillary Study

Upon approval of funding by the relevant peer review organization, fully developed protocols and peer review comments will be submitted back to the REPRIEVE ASC and EC for a final determination of impact and merit and detailed protocol review, including a review by the DSMB to insure that implementation of the fully funded, detailed peer reviewed protocol remains consistent with the goals of REPRIEVE. In all cases the EC will have final authority to request further development or final changes to an ancillary study. All ancillary studies must address any final protocol design issues prior to final REPRIEVE EC approval and implementation. Based on initial acceptance of the protocol by REPRIEVE, it is not anticipated that final approval will be withheld, but a detailed protocol incorporating peer review comments must be approved by REPRIEVE before implementation. An ancillary study that is approved will be developed as a co-enrolled study managed and overseen through the ACTG/DAIDS trial network in parallel with REPRIEVE, unless the ancillary study is proposing to request use of existing samples from REPRIEVE, in this case the ancillary study would not require a separate enrollment process. Proposals that are submitted for peer review but are not funded can be resubmitted for peer review. In such cases, the Investigative team will review the peer review comments with the ASC and again the ASC will review a detailed protocol before it is resubmitted for peer review.

9.0 Ancillary Databank Studies Proposing the Use of Already Collected Specimens

Ancillary studies that propose only to analyze stored specimens or images may also be put forth. Such proposals will be solicited toward the end of REPRIEVE (A5332). As above the ASC and REPRIEVE team will review concept sheets for approval. Consideration of merit, funding, peer review, and feasibility will be considered, as will impact on availability of stored blood. Approved concept proposals will be sent back to the proposing investigative teams for further development. As outlined above, final approval will be determined by the REPRIEVE team, after review of final protocol, analysis plan, funding sources, peer review, feasibility, etc. It

is anticipated there will be a high demand for valuable and limited blood, serum and plasma resources generated from REPRIEVE, and thus the ASC and EC will have to prioritize such proposals before approving them. Input from the Biomarker Committee will be solicited in this process. For studies which propose to use existing collected samples, the EC will take into consideration the scientific priority of the proposed ancillary study and the amount of extra blood available in REPRIEVE (A5332) before committing any blood for an ancillary study. In general, the REPRIEVE leadership will need to verify that required samples will be available, that the protocol is statistically sound, and that financial and data analysis issues are adequately addressed.

10. Data Analysis

Collection and analyses of the data will be carried out by or under the direct supervision of the Data Coordinating Center (DCC) and adequate funds should be requested for this purpose. The data base will not be released to an investigator outside the DCC framework, unless mandated by NHLBI policy with respect to Data Sharing agreements in place pertaining to complete and analyzed data after the study is finished. Unless an exception is approved in advance, ancillary study data will become part of the REPRIEVE TRIAL database. In no case will study data for an ancillary study be unblinded prior to unblinding for REPRIEVE (A5332).

11.0 Oversight of Approved Ancillary studies

Proposals that have received final scientific review and approval by REPRIEVE will be placed on the REPRIEVE restricted website. The ASC and DSMB will review approved ancillary studies for progress annually. Ancillary studies are subject to the review, approval and ongoing oversight of the REPRIEVE DSMB. The ancillary study Principal Investigator must submit annual summaries of study progress to the REPRIEVE ASC. Annual summaries will be required prior to February 1 of each year so they can be included in annual progress reports to NHLBI and should include the number of samples/patients analyzed, preliminary results, any problems encountered, published abstracts and manuscripts, etc. At the annual review, the DSMB will recommend continued approval, termination, or request modifications/clarifications to the ancillary study to the Executive Committee. Ancillary studies will not be approved for continuation that compromise the progress of REPRIEVE (A5332) or the Mechanistic Substudy of REPRIEVE (A5333s), eg by impacting recruitment, blinding, and accomplishment of the primary goals of the study. Recruitment and existence of ongoing ancillary funding will be taken into consideration during annual review of ongoing ancillary studies.

12.0 Publication of Ancillary Studies

Proposals for abstracts and manuscripts from the ancillary studies must be sent to the REPRIEVE Publications Committee for review and approval in a manner similar to other REPRIEVE publications and presentations.

APPENDIX I. Call for Applications: REPRIEVE Ancillary Studies

I. Jurisdiction

The **Executive Committee (**EC) will appoint the members and chair of the Ancillary Studies Committee (ASC).

The ASC will perform initial evaluation of all ancillary studies proposals and forward meritorious proposals for final approval by the EC.

II. Definition of Appropriate Ancillary Studies

Ancillary studies are investigations that are not part of the REPRIEVE main trial but that propose questions and test hypotheses that are relevant to the goals and purposes of the REPRIEVE trial.

Studies are of three types:

1) Studies which require recording of additional data elements and/or generation of additional data, i.e. imaging, biomarkers, genetic and outcome data, and physiologic measurements.

2) Studies that do not require generation of additional data but rather propose novel and incremental analyses not planned by REPRIEVE within or across studies using data collected in the course of the studies.

3) Studies using stored blood or images for analyses not envisioned or funded in the initial grant

III. Funding

The ancillary studies investigators are responsible for obtaining funding for their proposals and must outline a reasonable plan to obtain funding in the concept proposal and document adequate external funding or resources before final approval by REPRIEVE. This funding should include adequate funding to compensate the ACTG/DAIDS trial network for costs associated with implementation and monitoring of the trial as well as the CCC and DCC for costs associated with managing the substudy and storing and analyzing the ancillary study data. Studies proposing additional data collection (extra questionnaires, imaging, additional visits, blood tests, etc) as well as those merely needing additional statistical analyses will require adequate resources to perform the proposed tests and analyses. The Institutes of the NIH have programs designed to fund ancillary studies in clinical trials and exploratory/development research. These programs may or may not be a feasible avenue for those studies proposing to collect more data depending on timing of proposal, funding availability, and ongoing REPRIEVE recruitment. Investigators are encouraged to consider the timing of funding, as well other sources of funds. Funding may also be provided by ACTG itself, industry or by an investigator's institution.

Studies which propose only analysis of existing data within or across trials will also need additional funding to support analysis by the DCC. The extent of the funding required by

REPRIEVE for such analyses will be provide to the ancillary study investigators at an early stage, prior to concept approval and also during full protocol development. All analyses will be performed by the REPRIEVE DCC and the Trial will not provide data to potential investigators to do their own analyses.

Note that partnerships with industry must be discussed with the Reprieve ASC and NIH prior to *in-depth* discussions with the company. Once this brief discussion is complete, the investigator can submit their proposal and if chosen to be performed, the NIH and REPRIEVE leadership may be able to assist with negotiations with the company. REPRIEVE leadership will provide assistance in regards to potential conflicts with industry support, if any, as there may be restrictions inherent in such clinical trial agreements.

Please see the NIH guidelines for third party agreements
http://www.nhlbi.nih.gov/funding/policies/thirdparty.htm#ThirdParties

IV. Format of the Applications

See Attached

V. Timeline

REPRIEVE Ancillary study proposals will be reviewed semiannually on 4 occasions, beginning December 2014. Changes to this schedule may be implemented by the REPRIEVE ACS. For proposals originating within the ACTG, review by the ITSG will occur approximately one month earlier and successful proposals will be forwarded to the REPRIEVE ACS in December/May.

The REPRIEVE trial recognizes that some studies, particularly those that aim to recruit a smaller subset of REPRIEVE patients can start later than others and thus remains interested in meritorious, peer reviewed and funded proposals which can be accomplished within the overall recruitment timeline of REPRIEVE. The REPRIEVE ASC may elect to review semiannually, a limited number of such concept proposals up until the end of the enrollment period.

REPRIEVE ASC and EC will be charged with reviewing the ancillary study proposals and fully developed, approved proposals, to be sure that they are feasible and will not adversely affect the conduct of the principal studies and are statistically sound. The DSMB will also review the protocols for their scientific merit, safety and feasibility as discussed above.

VI. Additional Considerations / Frequently Asked Questions

a. The ASC/EC will provide input regarding adequacy of the proposed statistical methods and sample size calculations in their review of the protocols.

b. Individuals who are involved in the REPRIEVE Core Labs are encouraged to submit proposals for ancillary studies, which will be reviewed with the same procedures as outlined above. Core Laboratory Directors/Staff should not plan or perform additional studies outside the ancillary studies mechanism.

c. Ancillary study teams are required to work with a liaison on the REPRIEVE protocol team during full protocol development after approval of the initial concept proposal.

d. The ASC/EC will encourage investigators who are submitting proposals to form multidisciplinary teams including HIV and cardiology experts.

e. The ASC/EC hopes that many of the ancillary studies will be developed and reviewed by the site investigators and encourages the PIs and junior investigators to collaborate both within and across sites.

f. Collaborative proposals (from multiple REPRIEVE sites) are encouraged. If multiple proposals address similar scientific questions, the ASC/EC will encourage the investigators to work together to draft and submit a revised collaborative proposal.

APPENDIX II: REPRIEVE Study Objectives

REPRIEVE (A5332) Primary Clinical Objective

- To determine the effects of pitavastatin as a primary prevention strategy for major adverse cardiovascular events (MACE) in HIV.

REPRIEVE (A5332) Secondary Clinical Objectives

- To evaluate the effects of pitavastatin on each of the components of the primary composite MACE endpoint and all-cause mortality.
- To determine the effects of pitavastatin on LDL and non-HDL cholesterol in the HIV population and assess the relationship of changes in LDL and non-HDL to the incidence of MACE events.
- To evaluate whether baseline traditional risk factors (including smoking, blood pressure, dyslipidemia, glucose) and time updated HIV specific (immunological and virological) risk factors are predictive of MACE and pitavastatin effects on MACE in the HIV population.
- To evaluate whether baseline and time updated inflammatory and immune activation biomarkers are predictive of MACE and pitavastatin effects on MACE in the HIV population.
- To determine the effects of pitavastatin on the incidence of serious non-cardiovascular events and AIDS-defining events.
- To determine the safety of pitavastatin in the HIV population, including the development of diabetes mellitus, liver dysfunction, and myopathy.
- To collect blood to enable the evaluation of the relationship of host genetics to study endpoints in subsequent ancillary studies.

Mechanistic Substudy of REPRIEVE (A5333s) Primary Mechanistic Objective

- To determine the effects of pitavastatin on the morphology and composition of non-calcified coronary atherosclerotic plaque (NCP), including the progression of plaque volume and whether these effects are modulated by markers of inflammation and immune activation.

Mechanistic Substudy of REPRIEVE (A5333s) Secondary Mechanistic Objectives

- To determine the effects of pitavastatin on the progression of high risk plaque features including low attenuation plaque and positive remodeling.

- To determine the effects of pitavastatin on detailed markers of immune activation, including immune function (CD4, viral load), immune activation (%CD14+CD16+ monocytes, sCD163, CD14, MCP-1 and T-cell markers), inflammation (Lp-PLA2, hsCRP, IL-6), coagulation (D-Dimer and tissue factor) and traditional CVD risk indices including detailed parameters of glucose homeostasis (insulin, glucose and related indices of insulin resistance such as HOMA-IR, HgbA1c).

- To determine the relative contributions of baseline and pitavastatin induced changes in HIV specific immune activation and traditional risk factors, including LDL, on the presence and progression of coronary plaque and high risk morphological features in HIV.

- To collect blood to enable the evaluation of the relationship of host genetics to study endpoints in subsequent ancillary studies.

APPENDIX III: Concept Proposal Application

Format of Proposal Concepts for REPRIEVE (A5332) Ancillary Studies

In addition to the science and proposed methods/approach, proposal concepts should also address the following:

1. Scientific Importance
2. Feasibility/Impact on Parent Trial
3. Proposed Funding Source and review Process
4. Multi-Disciplinary Collaboration (investigator teams should, whenever possible, be multi-disciplinary and include heart, lung and blood (HLB), HIV, and/or investigators from other fields). Applicants for ancillary studies are strongly encouraged to assemble multi-disciplinary teams to facilitate collaborations between HLB and HIV experts. In additions, the multi-disciplinary team should include at least one REPRIEVE (A5332) site PI or Co-PI. Multi-disciplinary scientific partnerships were a key recommendation from the 2012 NHLBI AIDS Working Group and would bring together the expertise of scientists adept at understanding approaches, mechanisms, and tools in the non-HIV population together with scientists that understand the complexity of HIV.

Proposal concepts should be limited to 4 pages (excluding references). The page distribution is at discretion of investigator but all sections must be adequately addressed.

They should include:

I. General Information

- Study Title: Descriptive title of the proposed clinical trial.
- Proposing Investigator(s): Name, title, institution, address, telephone and email address of the proposing investigator(s).

II. Structured Abstract – one page

- Opening Statements, a few sentences addressing:

  - Scientific Importance
  - Feasibility/Impact on Parent Trial
  - Proposed Funding Source (please identify any specific RF's and deadlines you will be responding to)
  - Funding Review Process
  - Multi-Disciplinary Collaboration

  - Background
  - Specific Aims and Hypotheses
  - Study design
  - Significance
  - Novelty from previous studies and primary paper/analysis

III. Proposal – maximum three pages

A.Background: Provide the rationale for the study and the hypotheses to be tested. Include any preliminary data if available. Preliminary data can include the work of your own laboratory or others, or can be a review of the relevant literature. The investigator should make a strong case that the patients in REPRIEVE (A5332) and its methodology are appropriate to test the hypotheses proposed.

B. Specific Aims and Hypotheses: These should be focused.

C. Significance: This section documents how the proposal extends our knowledge and is unique from the analysis planned in REPRIEVE (A5332) or previous relevant papers. The relevance of the proposed studies to the primary aims of REPRIEVE (A5332) should be discussed. Discussion should include consideration of whether findings could be published regardless of whether or not the analysis supported the proposed hypotheses.

D. Methodology: A detailed explanation of the technical aspects of proposed investigations is not required. However the proposal should include enough information to permit the determination that the methods to be employed will be appropriate and sufficient to address the aims.

E. Feasibility and Multi-Disciplinary Collaboration

1. <u>The impact of the proposal on enrollment and retention of patients in REPRIEVE (A5332) should be discussed.</u> Proposals likely to impede enrollment into the primary trial will not be recommended for approval.
2. Timeline for the study, enrollment goals, and the feasibility of completing this study on time and within budget.

3. Description of plans to facilitate communication and collaboration among multi-disciplinary investigator teams.

F. Statistical analysis and Power Calculations (brief)

G. Proposed Funding Review Process and Funding Mechanism

1. Where will this application be peer-reviewed?
2. What is the proposed funding mechanism?

8. Budget*:

1. Provide an estimated budget, including direct and indirect costs; describe how the budget will adequately support obtaining the proposed data or performing the proposed analyses, including support of the REPRIEVE Data Coordinating Center and Clinical Coordinating Center personnel and infrastructure involved, a detailed budget is not required at this time.

9. References

***NHLBI Funding Opportunities**

Please note that as of fall 2014, the following NHLBI funding opportunities are available for REPRIEVE (A5332) ancillary studies addressing HIV-related HLB disease: 1) RFA-HL-14-023 "Clinical Research in the Prevention, Diagnosis, and Treatment of HIV-Related Heart, Lung, and Blood (HLB) Diseases in Adults and Children" (R01); 2) RFA-HL-14-024 "Basic Research in the Pathogenesis of HIV-Related Heart, Lung, and Blood (HLB) Diseases in Adults and Children" (R01); and 3) RFA-HL-14-029 "Basic Research in the Pathogenesis of HIV-Related Heart, Lung, and Blood (HLB) Diseases in Adults and Children" (R21).

APPENDIX IV: Ancillary studies proposal review template

Author	TITLE	Date submitted

Score [1 (best)-5]	Overall Considerations	Comments
_____	**Significance** Publishable as a standalone paper?	
_____	**Relevance to REPRIEVE** Nonoverlapping/Unique No planned subgroup analysis in that area	
_____	**Approach** Rationale clearly laid out Question clearly stated Data are available Power considered and justified Statistical analysis appropriate Appropriate regardless of findings of main study	
_____	**Funding and feasibility** Burden to the trial—administrative (including with respect to any sponsors), site, patients (including safety concerns), sample availability Adequate funding secured/anticipated	
	Other Concerns	
	Overall Priority --- NOT AN AVERAGE OF ABOVE - 1-2 high priority	

3 only after higher scoring proposals or only if revised

4only if extensively revised

>5 not worthy of pursuing or too close to primary analysis

General Comments

1

2

3

APPENDIX V Co-enrollment of REPRIEVE participants in single-site, on-site studies with ultimate goal of assessing statin effects on site-specific study endpoints

Investigative teams may petition the REPRIEVE leadership to co-enroll REPRIEVE participants in approved single-site stand-alone studies that are independent of REPRIEVE, with the ultimate goal of leveraging REPRIEVE study participants and data collected through REPRIEVE to answer critical questions for the field. REPRIEVE will permit co-enrollment into these smaller independently-funded studies as long as they do not interfere with REPRIEVE study visits or the collection of data for REPRIEVE. The study should not create an undue burden on REPRIEVE participantsor interfere with REPRIEVE study endpoints. Moreover, REPRIEVE will entertain requests for data sharing, eg to enable full phenotyping or to assess statin specific effects on unique site-specific endpoints, as necessary for each study, based on key principles set forth below.

Interested site investigators should submit to the REPRIEVE Ancillary Study Committee a two page executive summary of their proposal. This summary should include: a) study aims b) primary and secondary study endpoints c) flow diagram of study with key interventions and procedures and timing of interventions/procedures d) study population e) feasibility of co-enrollment f) potential effects of co-enrollment on REPRIEVE endpoints g) anticipated effects of statins on study endpoints h) study team i) study funding j) timeline for study completion k) details of the data to be requested after completion of REPRIEVE.

If the REPRIEVE Ancillary Study Committee approves the proposal, investigative teams may co-enroll REPRIEVE participants.

REPRIEVE blinding code will not be shared with investigative teams until after the main REPRIEVE study is completed/unblinded.

Investigative teams may petition the REPRIEVE team for sharing of select data elements, and permission will be subject to review and approval by REPRIEVE leadership.

Publications which depend on knowledge of the REPRIEVE blinding code and/or any REPRIEVE data may not be published by the investigative team without prior review and approval by the REPRIEVE trial team.

Interested site investigators should submit their executive summary of their proposal to:
Kathleen Fitch, MSN, Project Manager REPRIEVE Clinical Coordinating Center
Email: kfitch@partners.org