NASH CRN Pilot and Feasibility Studies Committee (Jan 04)

Contents

NASH CRN Pilot and Feasibility Studies Committee (Jan 04)

1. Background

The Nonalcoholic Steatohepatitis Clinical Research Network (NASH CRN) studies comprise a large and well characterized sample of individuals with various stages of nonalcoholic fatty liver disease, including steatosis, steatohepatitis, and cirrhosis. To make the best possible use of this resource, the NASH CRN Steering Committee encourages NASH CRN investigators to develop pilot and feasibility studies.

2. Definition of pilot and feasibility study

A pilot and feasibility study is carried out using NASH CRN patients or related materials, but is not a required part of NASH CRN activities. A pilot and feasibility study involves collection of new data, e.g., a new assay on a NASH CRN specimen or a new questionnaire for completion by NASH CRN patients.

The NIDDK will provide modest research support for NASH CRN investigators to explore the feasibility of a concept and to generate sufficient data to pursue it through other funding mechanisms such as R01 and R03. This support will be typically under $100,000 for a limited time (one to two years). The intent of these small awards is to obtain preliminary data for high risk new ideas. The pilot and feasibility studies are intended to: (1) provide initial support for new investigators, (2) allow exploration of possible innovative new leads or new directions for established investigators.

A pilot and feasibility study will not use central resources of the NASH CRN such as those provided by the Data Coordinating Center or central repositories.

3. Pilot and Feasibility Studies Committee charge

The Pilot and Feasibility Studies Committee does the following:

- Develops the policy for review and approval of pilot and feasibility studies of the NASH CRN.
- Reviews applications for pilot and feasibility studies of the NASH CRN patients or materials and makes recommendations for approval or disapproval to the Steering Committee.
- Communicates the decision of the Steering Committee to the investigator proposing the pilot and feasibility study.
- Maintains a list of all proposed pilot and feasibility studies indicating approval status, initiation date, and participating centers.
- Reviews final reports after study completion.
- Provides annual reports of the Pilot and Feasibility Studies Committee's activities to the Steering Committee.

4. Pilot and Feasibility Studies Committee membership and voting

The Pilot and Feasibility Studies Committee has six members: a chairperson (initially appointed by the NIDDK and, thereafter, elected by the Steering Committee), 3 clinical center principal investigators or co-principal investigators, one investigator from the Data Coordinating Center, and an NIDDK representative. The chairperson and 3 members from the clinical centers serve for 2 year terms. The members from the Data Coordinating Center and NIDDK serve for the duration of the NASH CRN.

Each Pilot and Feasibility Studies Committee member has one vote. In case of a tie vote, the Steering Committee will decide by mailed ballot if a meeting or conference call is not imminent. If a Pilot and Feasibility Studies Committee member proposes a pilot and feasibility study, he or she will be excused from reviewing that pilot and feasibility study proposal.

5. Operation of the Pilot Feasibility Studies Committee

The Pilot and Feasibility Studies Committee is a subcommittee of the Steering Committee. The Data Coordinating Center supports the operations of the Pilot and Feasibility Studies Committee by arranging Committee conference calls, receiving submitted applications for pilot and feasibility studies, administering the process for review of submitted applications, writing correspondence for the Committee, and maintaining the lists of pilot and feasibility studies and the document and correspondence files relating to the Committee's activities. The Data Coordinating Center relies on the principal investigator for each pilot and feasibility study and the Pilot and Feasibility Studies Committee members in completion of these activities.

Investigators wishing to conduct a pilot and feasibility study must complete an application. The Pilot and Feasibility Studies Committee will review the application for scientific merit (using the expertise represented by the Committee) and will assess whether the pilot and feasibility study represents undue burden for NASH CRN patients or could interfere with completion of the NASH CRN objectives. The Pilot and Feasibility Studies Committee will make a recommendation to the Steering Committee as to whether the pilot and feasibility study should be approved; the Steering Committee must approve the pilot and feasibility study for it to proceed. Investigators who are responding to a program announcement or applying for funding should gain the Steering Committee approval for the pilot and feasibility study before submitting their application to the funding organization.

6. Proposing a pilot and feasibility study

A pilot and feasibility study is proposed to the NASH CRN by submission of a completed NASH CRN Study Proposal (SP) form to the Pilot and Feasibility Studies Committee in care of the Data Coordinating Center. This form is available on the private view portion of the NASH CRN website

(www.jhucct.com/nash/closed/cmac/forms/admin/sp.pdf). The purpose of the form is to allow the NASH CRN Pilot and Feasibility Studies Committee to understand exactly what NASH CRN resources are wanted so that assessments of scientific merit and the impact or burden of the pilot and feasibility study on the NASH CRN patients and study group can be made.

Completion of this form will require specification of the following information:

- The principal investigator for the pilot and feasibility study.
- Names of other key investigators for the pilot and feasibility study and their institutional affiliations.
- The study title, objective, and estimated start and end dates.
- A concept sheet describing the research design and methods for achieving the study objectives (2 page maximum length – this is to be a concise, well organized description).
- The NASH CRN resources which the pilot and feasibility study wishes to use need to be specified in detail:
  - New data items or measurements to be collected on NASH CRN patients;
  - Any existing NASH CRN data that will be required;
  - Number of patients involved;
  - Quantity of specimens to be collected from patients and the conditions of specimen collection;
  - If access to previous NASH CRN specimens is needed for new determinations, specify the quantity and amount of specimens to be used;
  - Frequency of visits, patient contacts, or specimen collection;
  - Types of interview questions, physical measures, patient contacts, or specimen collection;
  - If access to previously collected NASH CRN data is requested (eg, measures on specimens or patients, treatment information), the data items must be specified by form name and item number.
- The primary outcome variable and sample size must be specified and, if possible, justified.
- An acknowledgment that the NASH CRN pilot and feasibility studies policy, including the policy on publications and presentations arising from pilot and feasibility studies, applies to the pilot and feasibility study.

The pilot and feasibility study activities that use NASH CRN resources may not proceed until the NASH CRN has approved the pilot and feasibility study.

Investigators participating in a pilot and feasibility study need IRB approval for the pilot and feasibility study at each site using a separate pilot and feasibility study consent form. Consent for the pilot and feasibility study cannot be part of any NASH CRN consent – pilot and feasibility studies are separate from the NASH CRN by definition. Notice of IRB approval of the pilot and feasibility study and a copy of the IRB approved consent must be provided to the Pilot and Feasibility Studies Committee prior to

initiation of pilot and feasibility study activities at the NASH CRN site (IRB approval is not required for review of a pilot and feasibility study application). The Data Coordinating Center will maintain a file of pilot and feasibility study IRB approvals and IRB-approved consents.

Confidentiality of individually identifiable data about NASH CRN participants must be assured. The NASH CRN provides no assurances that pilot and feasibility studies will be able to identify and contact NASH CRN participants in the future, particularly after the NASH CRN ends.

7. Review process for proposed pilot and feasibility studies

The Data Coordinating Center will circulate the submitted pilot and feasibility study application to the members of the Pilot and Feasibility Studies Committee with instructions that they are to send their comments (see below for what they are to comment on) to the chair of the Pilot and Feasibility Studies Committee by a specified date. The chair will collate the comments quarterly and prepare a written memo to the Steering Committee specifying the Pilot and Feasibility Studies Committee's recommendation for approval or disapproval. The Steering Committee will review that recommendation at their next meeting or conference call and make a decision for approval or disapproval. The principal investigator of the pilot and feasibility study will receive a copy of the memo directing the Pilot and Feasibility Studies Committee to review the study application (so that they know the time frame for review) and a copy of the memo from the Steering Committee specifying the decision for approval or disapproval.

Pilot and Feasibility Studies Committee members will be asked to assess the following:

- Whether the study has sufficient scientific merit.
- Whether the study would interfere with other NASH CRN activities.
- Whether the study would hamper continued recruitment or participation in the NASH CRN.
- Whether the study is consistent with the NASH CRN aim of facilitating a broad range of research.

Approved pilot and feasibility studies must be initiated within one year of being approved, or the approval will be withdrawn; this will allow recycling of resources allocated to a pilot and feasibility study that does not go forward, eg, due to failure to obtain funding. The principal investigator of the pilot and feasibility study will receive written notice 2 months before a pilot and feasibility study's approval is due to expire.

If two or more projects are submitted in the same quarter that propose the same or substantially similar work, the Pilot and Feasibility Committee will discuss both proposals by conference call or meeting and agree by simple majority vote which of the proposals to recommend. A Pilot and Feasibility Committee member will discuss the potential conflict at the next Steering Committee meeting or conference call with the Pilot and Feasibility Committee's recommendation regarding which one of the applications will be funded. The Steering Committee may override the decision of the Pilot and

Feasibility Committee and choose an alternative application for support or supporting of more than one application by simple majority vote.

If an application is received for a project that duplicates a project that was submitted earlier by another investigator, the application will be discussed by the Pilot and Feasibility Committee and usually turned down. The situation will be discussed at the next Steering Committee call or meeting. The decision by the Pilot and Feasibility Committee can be overridden by a simple majority vote of the Steering Committee.

If a major change occurs to a pilot and feasibility study's protocol after it has been approved (eg, addition of a visit, addition of a specimen, or addition of a measurement on a NASH CRN specimen – something that affects the impact on the NASH CRN participant or resource used), the Pilot and Feasibility Studies Committee must approve the change before it is implemented. The Steering Committee will be asked to approve the alterations, based on the recommendation of the Pilot and Feasibility Studies Committee.

8. Publications, abstract and presentations arising from pilot and feasibility studies

Publications arising from pilot and feasibility studies do not need to be approved prior to initiation; however, publications arising from pilot and feasibility studies must be reviewed by the Presentations and Publications Committee prior to journal submission; the purpose of the review is to assure that any statements about the NASH CRN protocol are accurate and that the NASH CRN resources used in the pilot and feasibility study are appropriately acknowledged. The process for review will be as follows:

- The draft manuscript should be sent to the Presentations and Publications Committee; the authors should specify the target journal.
- The paper will be circulated to the Steering Committee for voluntary comment direct to the corresponding author.
- The chair of the Presentations and Publications Committee will identify an internal reviewer for the paper and send the paper to that individual with a deadline for response; the reviewer will send his/her review to the chair of the Presentations and Publications Committee.
- The reviewer will review the paper for accuracy of statements about the NASH CRN resources used in the pilot and feasibility study and for appropriate acknowledgment of the NASH CRN.
- The chair of the Presentations and Publications Committee will send a written review to the author.

Abstracts and presentations arising from pilot and feasibility studies will not require approval from the NASH CRN. However, the NASH CRN would welcome being informed about such presentations and would provide review of materials if requested. It is expected that any presentation from a pilot and feasibility study would include appropriate acknowledgment of the NASH CRN resources used by the pilot and feasibility study.

NASH CRN Pilot and Feasibility Studies Committee (Jan 04)

Authorship for publications and presentations from pilot and feasibility studies is in the hands of the pilot and feasibility study group. It is expected that conventional authorship will be used, with an acknowledgment of the NASH CRN.

Access by pilot and feasibility studies to NASH CRN data collected on participants in the pilot and feasibility study will be governed by the Steering Committee and administered by the Data Coordinating Center. It is likely that access to baseline data from a NASH CRN study will be permitted to a pilot and feasibility study prior to the conclusion of the NASH CRN study, but only after the NASH CRN has determined that the baseline data are of a quality suitable for sharing. Follow-up data and information about treatment assignment for data derived from a NASH CRN clinical trial are unlikely to be available until after the NASH CRN study has ended, regardless of the timing of the pilot and feasibility study. Pilot and feasibility study investigators should be aware that there may be delays of possibly years between when their study ends and NASH CRN data are released.

NASH CRN data sets use the NASH CRN Patient ID number to link patient records. Pilot and feasibility study investigators should request data on the NASH CRN participants in their study by providing the NASH CRN ID numbers of the patients whose data are requested. The Data Coordinating Center will accept SAS, Excel, Access, ASCII, and other data files of records of NASH CRN ID numbers (word processer files are not acceptable, other identifiers are not acceptable).

The NASH CRN data which have been approved for provision to the pilot and feasibility study will be provided in SAS data sets using whatever SAS version is in use at the Data Coordinating Center'. Pilot and feasibility study investigators should be prepared to deal with SAS data sets.

A final report should be submitted to the chair of the Pilot and Feasibility Committee within 6 months of completion of the project. The final report should be limited to 1-2 pages and contain the following information:

- Name of the principal investigator
- Study title
- Start and end dates of funding
- Brief statement of findings
- Assessment of whether these results will lead to further investigation.

The final report will be reviewed by the chair of the Pilot and Feasibility Committee and distributed to the Data Coordinating Center for record keeping. The results will be presented to the Steering Committee by the principal investigator either during a Steering Committee meeting or conference call. The discussion of the study results should occur during the funding period or no later than 6 months after reaching the end of funding date.