24. HFM Study Ancillary Studies

24.1 Purpose

To enhance the value of the HFM Study, the Steering Committee welcomes proposals from individual investigators to carry out ancillary studies in collaboration with the HFM Study investigators.

24.2 Definition of Ancillary Study

An ancillary study is one based on information, images or biospecimens from the HFM Study participants in an investigation that is relevant to, yet not described in the HFM Study protocol, and derives support from non-HFM Study funds. It is anticipated that a typical ancillary study will propose the collection of additional data not collected or analyzed as part of the HFM Study parent data set.

24. 3 Ancillary Study Principles

1) Participation in, and approval of, an ancillary study is subject to review by the HFM Study Publications and Ancillary Studies (PAS) Committee. See Section 23.1 for composition of the PAS Committee. Also, the HFM Study External Advisory Committee is notified of all ancillary studies.

2) Approval by the PAS Committee will be defined as a majority of votes in favor of the proposal. In the case of an ancillary study which includes subject participation at all clinical centers, two-thirds approval of the PAS Committee membership will be required. Furthermore, the centers participating must each approve.

3) An ancillary study must receive Steering Committee approval before a grant to support it is submitted to a funding agency or to local institutional authorities (e.g., IRB), and before the study is permitted to begin.

4) All HFM ancillary study proposals initiated by a non-HFM investigator as PI must include as a Co-investigator at least one HFM Study PI or Co-investigator.

5) Ancillary studies require external (non-HFM Study) funding. Any ancillary study must have sufficient funding to cover the costs incurred by the HFM Study Clinical Centers and Cores (e.g., to process or ship samples), and the Data Coordinating Center (DCC) (for tasks such as sample selection, data management, preparing and documenting analysis files, participating in statistical analysis, and integrating the new ancillary data into the combined HFM Study database). Also, studies using Repository biospecimens must have adequate support for handling and using the specimens. Special consideration will be given to requests for ancillary studies to be funded through training grants or career development awards through the NIH or other peer-reviewed funding sources.

6) Considerations for approval of ancillary studies

The proposed study:

A) must meet requirements of the highest scientific merit.
B) must not, or minimally, interfere with the completion of the main objectives of HFM Study.
C) must not, or minimally, adversely affect participant cooperation or compliance with HFM Study.
D) must not create a serious diversion of HFM Study resources.
E) must put minimal demand on scarce HFM Study resources, such as blood samples.
F) must require the unique characteristics of the HFM Study patient data to accomplish its goals.
G) must have adequate resources to effectively complete the project.
H) must agree to provide the ancillary data to the HFM Study (also see 10 and 13).
I) must not jeopardize the public image of the HFM Study.
J) consider using the entire cohort for testing, rather than individual centers or isolated subgroups when appropriate.

7) Once an ancillary study is approved, if a change occurs in the structure or concept of the study (for example as a result of the NIH review process), including any change in data elements to be collected or analyzed, or any change to study aims, such changes must be disclosed to the PAS Committee and the HFM Study Steering Committee, for review and approval before the proposal is (re-)submitted to a funding agency.

8) A written progress report on ancillary studies must be made periodically (e.g., at time of Steering Committee meetings) to the Steering Committee.

9) All data collected under the auspices of an ancillary study is expected to adhere to the same high standards of quality applied to data collected in the core HFM Study. A plan for quality control must be submitted to the DCC for funded studies. In addition, once the ancillary study is initiated, periodic quality control reports must be sent to the DCC.

10) Data from ancillary studies will be made available to the DCC either on a real time basis using direct data entry into the DCC's computer server or through periodic transfers of ancillary data to the DCC.

11) Images, tracings and biosamples may usually be kept by the ancillary study investigators. During the HFM Study operation, further use of the samples beyond the objectives that have been approved by the PAS is prohibited without additional consent from the PAS Committee. The restrictions on specimens imposed by the Veterans Affairs for specimens collected at the VA sites must be observed. Also, the NIDDK has the option to require that the images, tracings (or copies of) and remaining biosamples be transferred to the NIDDK Repository at the end of the HFM Study.

12) Unless specifically arranged, all analyses will take place at the DCC and be conducted under the supervision of its biostatistician-investigators in collaboration with the ancillary study investigators. Under specifically approved circumstances, datasets will be released to external investigators for local analysis.

13) Proposals for abstracts and manuscripts resulting from all ancillary studies shall be submitted to the PAS for review and approval before establishment of a writing committee or a submission for publication or presentation. It is anticipated that principal investigators of approved ancillary studies will lead at least one scientific paper emerging from the ancillary study analyses.

14) An archival copy of the collected data and/or laboratory results not already held at the DCC will be sent to the HFM Study Data Coordinating Center at the conclusion of the data analysis and publication of the main ancillary study results. This transfer is the responsibility of the ancillary study HFM Study collaborator(s). Once transferred back to the HFM, these ancillary data will become part of the aggregate HFM Study data.

15) Information about proposed ancillary studies, and progress and results from approved ancillary studies are considered to be confidential and are not to be shared with others outside of the HFM Study except as provided for by the HFM Study Publications and Ancillary Studies Policy. Ancillary study investigators can share information among their co-investigators and with HFM Study investigators.

24.4 Funding of Ancillary Studies

Ancillary studies will not be funded by the HFM Study, but will require an independent source of funding.

24.5 Approval Procedures

1. Proposals may be generated by a participating clinical center or by other interested investigators providing at least one HFM Study PI or Co-investigator is included as a co-investigator. These applications are submitted to the Data Coordinating Center for review by the HFM PAS Committee.

2. There will be a two-step review by the PAS Committee. The first step is to have the proposal reviewed for its concept and general acceptability. This will be done in 2-4 weeks after submission. A short description of the study including the following information should be submitted.

a. Hypotheses to be tested.
Specific outcome variables that will be assessed.
Need for data and specimens from the DCC or Repositories.

b. Significance of the proposed ancillary study.

c. How will performance of this ancillary study affect the HFM Study?
Specifically:

i. Will there be any data/specimen/image collection beyond that specified in

the HFM Study protocol? If so, what additional information/samples will be obtained? What, if any, impact will this additional information/sample have on the main study?

ii. How much additional participant burden and time will be required to complete this ancillary study?

iii. Will additional funds be requested for the study and what will their source be?

3. If this proposal is acceptable in concept to the PAS Committee, a more detailed proposal should be written and submitted for review. This proposal should include detailed information on:

a. Hypotheses to be tested.
b. Background and significance of the study.
c. Conduct and performance of the study including specifying the study population and the data to be collected.
d. HFM Study staff and DCC burden. Costs for this work need to be included in the project's support.
e. Sample size justification.
f. Quality control of the data.
g. Data analysis methods.

4. The PAS Committee will review the proposal within 2-4 weeks. The decision can be for approval, modifications with further review, or disapproval.

24.6 Publication of Ancillary Study Results

The policies regarding publications and presentations of the result of ancillary studies are the same as those governing the publications and presentations of results of the main study (see Section 23). These policies are designed to:

1. Assure timely publication of the results to the appropriate professional audiences.
2. Avoid premature publications of results that might compromise the performance of the main study or that might compromise the ability to publish the results in high quality peer reviewed journals.
3. Maintain high standards of the published material.
4. To guard against duplicate publication of results, unless in review articles after the results have been published in a peer-reviewed article.
5. Assure equitable attribution of credit to all of the professionals participating in the ancillary study and the HFM Study.