NCI, Division of Cancer Prevention
Community Oncology and Prevention Research Group

Protocol Information Office

Procedure: Submission, review, and tracking of Ancillary Studies to DCP/PIO

Date: 12/17/02

Purpose:

Implement a standard process for the submission, review, and tracking of ancillary studies submitted by CCOP Research Bases.

Background:

The Division of Cancer Prevention encourages ancillary studies of scientific merit as a way of maximizing the efficiency of clinical trials. An ancillary study is a separate study utilizing all or part of the population of subjects in an existing study supported by DCP. An ancillary study can supplement the main study by collecting data on a separate endpoint (e.g. a different cancer or noncancer disease outcome; quality of life); collecting additional information on subjects (e.g. clinical, laboratory, biorepository specimens, or risk factors); utilizing biorepository specimens for analysis, or introducing a new intervention for evaluation (e.g. screening test). An essential element of an ancillary study is that it not compromise scientific validity or feasibility of the main study. Investigators should submit a protocol for an ancillary study only after approval and activation of the main study.

The Division welcomes ancillary studies for endpoints unrelated to cancer, but it expects that investigators receive funding outside of DCP to support such studies. Ancillary studies with an endpoint relevant to cancer might have also received funding outside the CCOP mechanism (e.g. R01 grant). When a proposed ancillary study has received approval through peer review for funding through a Government source, DCP will review the study as a protocol and will focus its review on the feasibility of conducting the study in the CCOP network without compromising the feasibility or scientific validity of the main study. When a proposed study has not received approval through a peer review, DCP will conduct its usual two-step review of a concept followed by a protocol.

Process:

1. DCP encourages investigators to contact program directors in the Community Oncology and Prevention Trials Research Group (COPTRG) prior to submitting a concept or protocol for an ancillary study.
2. As with all CCOP studies, the CCOP Research Base is the only institution able to submit a concept or a protocol. The Research Base should have processes in place for development and internal review of a proposed study before submitting the ancillary study to the DCP Protocol and Information Office (PIO) as a new study (and not as an amendment to the main study). An accompanying cover letter should describe the benefits from the proposed ancillary study, defend the need to conduct the research as an ancillary study instead of a separate study, and state how the ancillary study will affect the conduct of the main study.

3. The concept should include all the components of a usual concept submitted to DCP. The following is a list of components with comments specific to ancillary studies:
    1) Background: In addition to the rationale and scientific justification supporting conduct of the ancillary study, include a description of the main study and details regarding the integration of the ancillary study.
    2) Objectives: Limit to the ancillary study
    3) Hypotheses: Limit to the ancillary study
    4) Study Design: Clearly differentiate procedures that are required for the ancillary study (even if they are also being performed as part of the main study) from procedures being done in the main study. If the sample size for the ancillary study is less than for the main study, indicate how subjects will be chosen for the ancillary study.
    5) Statistical Section: Although the statistical section for a concept is not as extensive as that for a protocol, provide data to support the sample size required to address the Objectives of the ancillary study. This sample size can be less than the sample size for the main study. This section should also indicate the methods to be used to analyze the data.
    6) Budget: If the ancillary study requires funding for components not covered by the CCOP grant, the concept should be accompanied by a budget together with explanation for the source of that funding.
    7) Supporting Documents: If some components of an ancillary study will receive support from a mechanism other than the CCOP program (e.g. R01 grant), the investigator should submit a copy of relevant applications and reviews.

4. The protocol should include all the components of a protocol submitted to DCP. The following is a list of components with comments specific to ancillary studies:
    1) Background: same as for concept
    2) Objectives: same as for concept
    3) Hypotheses: same as for concept
    4) Study Design: same as for concept
    5) Sample Size: Provide data to support the sample size required to address the Objectives of the ancillary study. This sample size can be less than the sample size for the main study.
    6) Statistical Plans: Limit to methods for analyzing data in the ancillary study related to the objectives and hypotheses of the ancillary study.
    7) Budget: same as for concept

8) Supporting Documents: same as for concept
9) Informed Consent: The consent form should contain all the components detailed in the NCI Informed Consent Recommendations and Template (http://www.cancer.gov/clinical_trials/doc_header.aspx?viewid=5fca4dc5-b6a7-4272-be96-b489f23022e5). The consent form should be specific to the ancillary study to prevent confusion with purposes, procedures, risks, etc. relevant to the main study. Furthermore, no part of the consent form for the ancillary study should be in conflict with the consent form already signed for the main study.

5. Procedures for processing protocol by Program Specialist in DCP PIO
   1) If any required elements are missing from the protocol, discuss with the Chair of the Protocol Review Committee to determine the proper course of action to obtain the required information. This may involve contacting the Research Base with communication documented in the file.
   2) Enter information about the ancillary study into PIMS, and the CCOP protocol review database as a new protocol.
   3) Prepare an arrival memo to the Chair of the Protocol Review Committee with a cc to COPTRG chief and to the Head, PIO.
   4) After determination by the Chair of the Protocol Review Committee that the protocol is suitable for review, the Program Specialist will set up a protocol review meeting.
   5) Where appropriate, Program Specialist will recommend as reviewers the original reviewers for the main study protocol. Otherwise, will recommend new reviewers based on the content of the ancillary study.
   6) Program Specialist will maintain for each ancillary study a file including copies of the protocol and all correspondence between the Protocol Review Committee and the investigators.
   7) Program Specialist will set up reviews for protocols revised in response to DCP's initial review. Reviews for revised protocols can take the form of a formal meeting or a paper concurrence review by all or some of the original reviewers, according to the judgment of the Chair of the Protocol Review Committee.
   8) PIO will submit a copy of the approved ancillary study protocol to PDQ.

6. Review of Protocol for Ancillary study:
   1) The Cancer Prevention and Control Protocol Review Committee will review the protocol for the ancillary study together with a copy of the main study. The Committee will pay particular attention to the following factors:
      1. Effect of the ancillary study on the scientific validity and feasibility of the main study
      2. Scientific rationale for the ancillary study
      3. Analysis of data
      4. Review of supporting documents (e.g. relevant grant applications and reviews)
      5. Human subjects issues, including informed consent
   2) The Chair of the Committee will send results of the review to the Principal Investigator of the Research Base, the Study Chair of the ancillary study, and the Study Chair of the main study. The review letter will take one of the following forms:
      1. Ancillary study approved

2. Request further information with submission of revised protocol
3. Ancillary study rejected, together with reasons for rejection.

Studies that are neither approved nor rejected will receive review letters containing issues to be addressed in a cover letter accompanying a revised protocol. The CCOP research base must submit revised protocols with accompanying cover letters to the DCP PIO. The Review Committee will review the revised protocol and report its results in a manner similar to the results of the initial review. Investigators cannot begin conducting an ancillary study until they receive protocol approval from the Committee.

3) The Cancer Prevention and Control Protocol Review Committee will determine the credit assignment for the ancillary study, which will be included in the protocol approval letter. An ancillary study may or may not receive credit in addition to credit received from the main study. Factors affecting the credit assignment include the relevance of the ancillary study to cancer prevention or control, the presence of other funding, and the amount of data management required for conducting the ancillary study in addition to the data management already required for conducting the main study.