Chapter 12: Ancillary Studies Policy

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12.1 Introduction

To enhance the value of the CAMEO Clinical Trial, the CAMEO Executive Committee welcomes proposals from individual investigators to carry out CAMEO ancillary studies. Ancillary studies must be reviewed and approved by the CAMEO Ancillary Studies Committee (ASC) and approved by the CAMEO Executive Committee (EC) before the inception or submission of an ancillary study proposal for external funding consideration.

12.2 Overall Goals and Objectives

The ultimate goals of the CAMEO study are to:

1) Explore the value of optimized anti-TNF therapy started within 6 months of diagnosis to achieve complete bowel healing
2) Identify clinical, endoscopic, histologic, and radiologic predictors of complete bowel healing in this setting which improved patient classification.
3) Identify additional host (genomic, immune, metabolic, transcriptomic) and microbial (metabolite profiles, metagenomics, metatranscriptomics, mucosal 16S sequencing) predictors of complete bowel healing in this setting which provide insight into mechanisms of anti-TNF response and nonresponse.

Ancillary studies may:

1) Make use of clinical, endoscopic, histologic, radiologic, and translational data collected during the CAMEO study

2) Generate new data elements from existing CAMEO clinical, endoscopic, histologic, radiologic, and translational data collected during the CAMEO study

3) Generate new host (genomic, immune, metabolic, transcriptomic) and/or microbial (metabolite profiles, metagenomics, metatranscriptomics, mucosal 16S sequencing) data from CAMEO biospecimens.

These may be studies which test hypotheses related to the overall goals of the CAMEO study, or studies which test new hypotheses unrelated to the goals of the CAMEO study which provide insight into mechanisms of pediatric CD pathogenesis.

12.3 Who can Submit and Participate

Applications for ancillary studies are encouraged from any CAMEO investigator and institution with the capability to perform the proposed studies, without restrictions. Applications from outside the CAMEO investigator group will also be entertained upon request.

Three types of investigators will be considered, with priority given to Type 1 and 2 investigators:

1. PI with proven track record of independent investigation related to IBD basic, translational, or clinical research, as evidenced by first or last author publications and/or independent funding.
2. PI at the career development stage of IBD research, with a mentor who meets the criteria in 1 above.

3. PI with a proven track record of independent investigation in a non-IBD area, as evidenced by first or last author publications and/or independent funding, who now seeks to apply those skills to answer an IBD question.

12.4 What Resources can be Requested?

In general, three types of resources may be requested. Projects which will utilize biospecimens, which represent a finite resource, will in general need to receive an outstanding impact score to receive approval by the ancillary studies committee. Projects which will only utilize existing data may be approved with an overall impact score in the very good to excellent range and may be more exploratory. **Careful attention will be paid to the amount of the biospecimen requested; in general, it should be less than 5% of the original amount in the tissue bank.**

To summarize ancillary studies should be clearly classified in the request to indicate that they will:

1. Only utilize existing clinical, endoscopic, histologic, radiologic, or translational data.
2. Generate new data elements from existing clinical, endoscopic, histologic, radiologic, or translational data.
3. **Generate new host or microbial translational data, using banked plasma, human genomic DNA, mucosal or fecal DNA, mucosal RNA, or banked stool samples**.

12.5 Timing of Submissions

Full proposals should be submitted to the ASC no less than 3 months prior to the planned date of submission to a funding sponsor to assure that ASC review, input, and approval can be provided in ample time to meet sponsor deadlines. The submission should also precede one of the established quarterly review meetings of the ASC by at least two weeks. If the intent is to submit for extramural funding to support the ancillary study, the proposal should be accompanied by an Aims page formatted for the planned funding agency. CAMEO will make every effort to complete review of such proposals by its ASC and Executive Committee within 4-6 weeks, allowing successful applicants 6-8 weeks to prepare and submit applications for funding. Note that additional detailed scientific reviews of such proposed ancillary studies that are submitted to NIH or foundations for funding will be conducted by the Study Sections that review the associated applications.

For proposals that will not undergo future rigorous, scientific peer-review, the deadline for receipt of the completed full proposal will be modified to include 8 weeks for the ASC to conduct its own scientific review.

Proposals for ancillary studies to CAMEO for which funding has already been secured or for which application will be made to some other potential funding source should be submitted to CAMEO for its approval at least three months prior to the intended project starting date, allowing CAMEO to conduct its own scientific review.

12.6 Executive Committee Review

During ASC review, all ancillary study proposals will be circulated to the CAMEO Executive Committee for comment. Interested CAMEO investigators may contact the PI of the proposed ancillary study and request to participate as collaborators in the study. In addition, as appropriate, the ASC may recommend that the ancillary PI consider adding additional sites to provide added power, a more diverse population, or to contribute specific scientific expertise.

12.7 Funding

There is no direct cost to the ancillary study for biospecimens but there will be a charge for aliquoting and shipping. All additional costs for the ancillary study will be borne by the investigators conducting the ancillary study. UNC DCC costs for collecting and cleaning additional data, data transfers, and data archival should be included in the ancillary study budget. Before applying for external grant funding using biospecimens from CAMEO, investigators must receive an approval letter for their ancillary study proposal. The level of funding requested must be sufficient to support the additional data collection, management, and analysis required by the ancillary study. Investigators planning an ancillary study are encouraged to consult with the ASC during development of the proposal to ensure consensus on the resources required for the project. Funding of a grant proposal for an ancillary study at a reduced level from that proposed will likely require corresponding modifications to the work scope of the ancillary study. The ASC will review the proposed modifications before submitting it to the Executive Committee for final approval, as outlined in the instructions below.

ASC approval of a study is valid for twelve months and if, within twelve months of initial approval by the ASC, an investigator is unsuccessful in obtaining the necessary resources, including funding, the initial approval of the project will be withdrawn. If a proposal for extramural funding is scored but not funded, the investigator should share the proposal summary statement with the ASC, who may grant an additional twelve-month extension to the initial approval while a grant resubmission is prepared and reviewed.

12.8 Instructions for Preparing Ancillary Study Proposals

The “CAMEO Ancillary Study Proposal Form” is available on the CAMEO website under Guides and Templates/Data collection documents, Forms, Guides. Ancillary study proposals should not be longer than 7 pages and should include the following elements:

- Cover page with Project Title, Investigator Names and brief Abstract (<500 words). (1 page)
- Research Plans including Specific Aims/Hypotheses, Background and Significance, Research Design and Methods, sample size justification, and Statistical Analysis including: (3 pages)
    a. Sample size justification
    b. Participant selection criteria and consideration
    c. Advantages to using CAMEO cohort to answer research questions
    d. Recruitment and data collection methods
    e. Time burden, burden on participant, burden on clinic staff
    f. Proposed compensation

g. Results/alert reporting
h. Potential benefits of participation (if any)

- Description of specimen or data request (1 page)
    a. Specific types(s) of samples
    b. Volume of each sample
    c. Time of sample collection (baseline vs. post-baseline)
    d. Number of participants
    e. Proposed laboratory that will perform the assays
    f. DNA specimens – special needs should be delineated.
    g. Other required study data (e.g. baseline and/or follow-up data)
- Time table with key dates (grant submission, target date for receipt of specimens, and completion of study)
- Agreement to return any unused biological specimens and data sets
- Budgetary issues
    a. Source(s) of funding
    b. Draft budget – should describe costs related to:
        i. Space, personnel, equipment, and IRB approval
        ii. Statistical analysis and data management
        iii. Visits or examinations outside of the primary study protocol.

  PI should consult with DCC in preparing budget if their data management and analysis services are requested.
- NIH-style Biosketches for all Key Personnel. (No page limits).

All proposed ancillary studies must be reviewed and approved by the CAMEO ASC and the CAMEO EC before submission to a funding agency. See Section 12.5 regarding timing of submissions.

12.8.1 Review Process

Requests will initially be reviewed by the ASC, and assigned an overall impact score (below good, good, very good, excellent, outstanding) using the Ancillary Study Review Sheet, stored on the CAMEO website under Ancillary Studies, and recommendation of Approve, Disapprove, or Defer to the CAMEO Executive Committee. To ensure thorough scientific review, the Chair of the ASC may elect to seek outside expert opinion. The ASC will recommend approval or rejection to the Executive Committee or will request modification. The ASC will make every effort to complete review of proposals within 4 weeks. Quarterly deadlines for proposal submission will be posted on the CAMEO website.

A proposal, which receives an affirmative majority from the ASC, will be forwarded to the Executive Committee. The Executive Committee will have 4 weeks to authorize proposals approved by the ASC. A failure of the EC to provide an opinion back to the ASC will be considered an affirmative vote. Approval or disapproval in both the ASC and Executive Committee is based on majority opinion.

Projects which are not approved will be returned to the PI, without an option to re-submit. Projects which are deferred will be returned to the PI, with an option to revise and re-submit, one time. This process is modeled on the current NIH Study Section and Council system.

The investigator may only proceed with the ancillary study after he/she has received a formal approval letter from the CAMEO ASC. Any changes that occur in the structure or concept of an ancillary study that has been approved must be submitted to and reviewed by the ASC and Executive Committee according to the policies outlined for initial submissions.

Principal investigators of all ancillary studies will provide a written annual report to the ASC and Executive Committee on study progress.

12.8.2 Material Transfer Agreement

In all cases, PIs whose projects are approved by the ASC and Executive Committee for support of ancillary studies will require a bidirectional MTA with Emory University and DUA with the UNC DCC. A site conducting an approved ancillary study may share biospecimens with another laboratory at the same site if that sharing was part of the original proposal approved by the ancillary studies committee. If sharing with another laboratory was not part of the original ancillary study proposal, then the ancillary study site Principal Investigator must obtain clearance from the ancillary study committee prior to sharing specimens.

12.8.3 Human Subjects / Data Confidentiality

Confidentiality of CAMEO enrolled patients must be guaranteed. Individually identifiable data may not be released. If the data requested for an ancillary study is not covered in the original informed consent process for the main CAMEO, then a signed consent must be obtained from every participant in the ancillary study. Any investigator or personnel having access to CAMEO data must receive an orientation on the Trial's confidentiality policy. Key personnel of the ancillary study must be certified in the NIH OHSR or equivalent training course.

A copy of the IRB letter for the ancillary study should be sent to the Clinical Coordinating Center and Data Coordinating Center. If a separate consent form is required for the ancillary study, a copy of the signed ancillary study consent form for each study participant must be included in the CAMEO record. A data file tracking all signed ancillary consent forms must be maintained by the ancillary study and an electronic copy of that file must be delivered to the CAMEO DCC.

The principal investigator of an ancillary study will be responsible for monitoring the study to assure continuing compatibility with confidentiality and consent policies of CAMEO and providing written progress reports on the ancillary study.

12.9 Analysis and Publication of Results of Ancillary Studies

The site responsible for performing the statistical analysis of the ancillary study must be specified in the Ancillary Study application. Applicants are encouraged to contract data analyses with the UNC DCC. Ancillary studies funded as career or training awards as well as studies taking place in a subset of clinical sites will be situations in which data analysis might occur outside the DCC. These situations will require approval by the ASC and Executive Committee and the investigator of the ancillary study to provide interim reports on analyses to the DCC to ensure (1) consistency with data in the CAMEO database and (2) the quality of the analytic approach.

Since ancillary projects must involve at least one CAMEO investigator in a collaborative relationship, each abstract, presentation, and manuscript should also include CAMEO

investigators as co-authors to recognize their participation. The ancillary project lead should work closely with the Publications Committee to determine investigators who are eligible for authorship. This condition should be met unless extenuating circumstances exist that should be stated and justified as part of the *original submission to the ASC*. All publications, presentations, and abstracts derived from an approved ancillary study must acknowledge support from the CAMEO grant as well as the specific support for the ancillary study. All manuscripts that report CAMEO data must include the following statement: Research reported in this publication was supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health under Award Number U01 DK134356. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Proposals for manuscripts resulting from all ancillary studies must be submitted for review to the Publications Committee and will require approval by the EC prior to submission for publication or presentation. Publications reporting baseline data from an ancillary study will only be approved following the publication of the main study baseline manuscript. Publications based on outcome data will follow the primary study outcome manuscript. The phrase "CAMEO Clinical Trial" should be included in the title in all scientific presentations and manuscripts and listed as a key word whenever possible. Manuscripts should also contain an appendix listing CAMEO investigators when appropriate.

12.10 Handling of Cameo Clinical Trial Data and Specimens

At the time of distribution of CAMEO specimens and/or information, the CAMEO ASC, in coordination with the DCC, will make explicit arrangements with the ancillary study PI for the security of these study materials, and for their final disposition at the conclusion of the ancillary study. The safety and confidentiality of the CAMEO data at the collaborating institution is the responsibility of the ancillary study PI, as is the appropriate disposition of biological materials after the ancillary study has been completed.

12.11 Ancillary Study Data

An archival copy of the newly collected data and/or laboratory results not already held at the UNC DCC will be sent to the CAMEO DCC at the conclusion of the data analysis and publication of ancillary studies. The ancillary study must also provide appropriate documentation for the data to make it useful for outside investigators. Once transferred back to the CAMEO DCC, these ancillary data will become part of the aggregate CAMEO data and included in the NIDDK's limited access data program. Limited access data is made available to the public in accordance with the NIDDK Policy for Distribution of Data.

12.12 Ancillary Studies Committee Membership

The Chair of the ASC will come from the EC. Each ASC member will serve a 3-year term starting January 1 of their appointed year. Members may be considered for a second consecutive term by the CAMEO Executive Committee.

In addition, when needed, we will establish a panel of ad hoc reviewers in specific areas of expertise who are not CAMEO site investigators.

Table of Modifications

Version Date	Description of modification(s)	Modified & Reviewed By
05/16/2023	• First Publishing	N/A
7/28/2024	• Updated PROTECT policies to CAMEO	LAD
11/25/2024	• Reviewed with CAMEO EC and DCC	LAD
4/16/2025	• Updated Section 12.5 Timing of Submissions • Updated Section 12.8.1 Review Process	LAD