

# A-2: PROPOSALS REQUIRING RESIDUAL BIOLOGICAL SAMPLES FROM US PATIENTS

(To be completed after SC approval)

## Proposal Submission Form

### Proposal for use of NCTN Clinical Trial Bio specimens

Length limits: Sections 8-14 should be no more than 5 pages (not including instructional text).  
Sections 15-19 should be no more than 3 pages (not including instructional text).

Review timeline: Proposals received and accepted by PIO  $\geq 6$  weeks prior to the standing committee review date will be scheduled for the call 6 weeks hence pending review slot availability. If the committee agenda is full, it will be queued to the next available review slot.

#### ABSTRACT:

Please provide an abstract of your proposal in no more than 300 words: [Single-click here to add text]

#### ADMINISTRATIVE INFORMATION

##### 1. Submission type

Please mark the appropriate box with an "X".

Original submission

Revised submission

##### 2. Date: [Single-click here to add text]

##### 3. Title of proposed correlative study: [Single-click here to add text]

*Your study title must reference the protocol number[s] of the clinical trial[s] from which you are requesting biospecimens, and should be as descriptive as possible, similar to the level of descriptiveness required for titles of clinical trials.*

##### 4. Principal Investigator

Name of Principal Investigator of the proposed study: [Single-click here to add text]

Suffix (e.g., M.D., Ph.D.): [Single-click here to add text]

Network Group affiliation (if any): [Single-click here to add text]

Institution: [Single-click here to add text]

Mailing address: [Single-click here to add text]

Email: [Single-click here to add text]

Phone: [Single-click here to add text]

Name of IRB of record for this proposal: [Single-click here to add text]

## 5. Co-investigators

Only those investigators who have had/will have substantive input into the design, development, and/or conduct of your proposed correlative science study should be listed below.

- Please provide a **letter of collaboration** from each co-investigator.

Name: [Single-click here to add text]

Suffix (e.g., M.D., Ph.D.): [Single-click here to add text]

Institution: [Single-click here to add text]

State, Country: [Single-click here to add text]

Email: [Single-click here to add text]

Network Group affiliation (if any): [Single-click here to add text]

Name: [Single-click here to add text]

Suffix (e.g., M.D., Ph.D.): [Single-click here to add text]

Institution: [Single-click here to add text]

State, Country: [Single-click here to add text]

Email: [Single-click here to add text]

Network Group affiliation (if any): [Single-click here to add text]

Name: [Single-click here to add text]

Suffix (e.g., M.D., Ph.D.): [Single-click here to add text]

Institution: [Single-click here to add text]

State, Country: [Single-click here to add text]

Email: [Single-click here to add text]

Network Group affiliation (if any): [Single-click here to add text]

Name: [Single-click here to add text]

Suffix (e.g., M.D., Ph.D.): [Single-click here to add text]

Institution: [Single-click here to add text]

State, Country: [Single-click here to add text]

Email: [Single-click here to add text]

Network Group affiliation (if any): [Single-click here to add text]

Name: [Single-click here to add text]

Suffix (e.g., M.D., Ph.D.): [Single-click here to add text]

Institution: [Single-click here to add text]

State, Country: [Single-click here to add text]

Email: [Single-click here to add text]

Network Group affiliation (if any): [Single-click here to add text]

## 6. Network Group involvement

Will a Network Group collaborate on the proposed study? [ ] Yes [ ] No

If “Yes”: Name of Network Group: [Single-click here to add text]

## **7. Lead Organization**

Name of the lead organization for this proposed correlative study (for example, name of the institution, Network Group, or consortium): [Single-click here to add text]

Specific Aims: Objectives and Hypotheses

*NOTE: If your request is associated with a grant application with multiple Specific Aims, use this form to describe only those Aims that involve the use of the requested biospecimens.*

## **8. Objectives**

What are the objectives? *(Please distinguish primary and secondary objectives.)*

[Single-click here to add text]

## **9. Hypotheses**

What are the specific hypotheses?

[Single-click here to add text]

## **BACKGROUND AND SIGNIFICANCE**

### **10. Trial(s) from which biospecimens are being requested**

Protocol number(s) and protocol title(s) of the trial(s) from which biospecimens are requested:

[Single-click here to add text]

*Note: If you are requesting biospecimens from more than one trial, your proposal should provide a clear rationale for including biospecimens from each of the different trials.*

Number of cases for whom biospecimens were obtained in the trial: [Single-click here to add text]

Why are biospecimens from *this clinical trial* necessary to address your hypothesis? Please remember that data from large, randomized clinical trials should primarily be used to answer definitive correlative science hypotheses, as opposed to early biomarker discovery efforts. In your response, please briefly describe the trial(s) and its results, if available:

[Single-click here to add text]

### **11. Preliminary data and study justification**

Please provide preliminary data on your chosen marker(s) and assay(s) that motivate the stated primary objectives and justify the need for performing the proposed study. The justification should include a discussion of the potential for clinical utility of the marker(s) (e.g., prediction of resistance to taxanes): [Single-click here to add text]

## Research Design and Methods

### 12. Tissue/biospecimen type

What tissue/biospecimen types are you requesting? (e.g., FFPE malignant primary tumor tissue):

[Single-click here to add text]

Required number of biospecimens per specimen type: [Single-click here to add text]

How many cases in the trial currently have biospecimens? [Single-click here to add text]

How many cases will have material left for future studies if the requested biospecimens are provided for this study? [Single-click here to add text]

Will this study exhaust any blocks? [Single-click here to add text]

Required number and thickness of sections from each biospecimen (if solid tissue is requested):

[Single-click here to add text]

Required amount of other type of biospecimen (if biospecimens other than solid tissue are requested): [Single-click here to add text]

### 13. Laboratory methods

Description of laboratory methods: [Single-click here to add text]

Note: Your description of the laboratory methods should include the following:

1. Specify the analyte(s), technical platform, and sources of assay components (e.g., reagents, chips, and calibrators).
2. Demonstrate that the proposed assay methodologies are standardized and reproducible, and will work in the type of biospecimen requested.
3. Provide available data on the analytical performance of the assay – the accuracy, precision, concordance, reportable range and failure rate, as applicable; include a basic description of sample size and replication scheme from which analytical performance estimates were derived.
4. Describe the scoring system, and, if cutpoints will be used, specify the cutpoints and provide the rationale for the cutpoints selected.
5. Provide information on the use of positive and negative controls, calibrators, any critical preanalytic requirements, and (if applicable) how inter-laboratory variability will be assessed and minimized.

### 14. Facilities & personnel

Please explain who will be doing the laboratory work, in what role, and in what facility(ies):

[Single-click here to add text]

Please explain who will be responsible for the statistical and bioinformatic analyses of the data that will be generated in the proposed study: [Single-click here to add text]

#### *STATISTICAL CONSIDERATIONS*

Although it is recommended that this section be developed in consultation with a biostatistician, ideally a statistician who is familiar with the specific trial data elements relevant to the proposed correlative study, the exact nature and extent of the biostatistical collaboration is left to the investigator to define.

#### **15. Endpoints (outcomes)**

Precisely define the endpoints that are the subject of the study's main objectives; for time-to-event outcome variables, be sure to clearly indicate the types of events included in each endpoint definition:

[Single-click here to add text]

#### **16. Case selection**

Specify the proposed case selection method, including inclusion/exclusion criteria, and whether stratification or matching will be used, or state if you simply request biospecimens from all cases with adequate biospecimen available. If a complex case selection strategy (e.g., matched or adaptive selection) will be used, then the specific algorithm should be described:

[Single-click here to add text]

#### **17. Statistical analysis plan for addressing the primary objectives**

Statistical analysis plan: [Single-click here to add text]

Note: In your statistical analysis plan, describe how the primary objectives will be addressed in a quantifiable and statistically evaluable way. Indicate the specific quantities that will be evaluated and the general statistical framework (e.g., estimation, association, comparison, prediction).

In your statistical analysis plan, please also provide the following, as applicable:

- Statistical methods for the primary analyses (e.g., Cox proportional hazards regression, conditional or unconditional logistic regression, etc.).
- Transformations applied to variables.
- Methods for marker cutpoint validation.
- Variable selection procedures (including a list or description of the variables initially considered for inclusion in the model).
- List of standard clinical variables to be incorporated into models or other analyses.
- Multiple-comparisons adjustment methods.
- For complex studies, methods that will be used to validate the analysis results, or a rationale for not performing a validation study.

- Any other information necessary for the Committee to understand and evaluate the primary analyses you are proposing.

### **18. Statistical justification for sample size**

Based on the stated primary analyses and proposed statistical analysis plan, provide a justification (rationale) for the requested number of biospecimens.

Sample size estimate: [Single-click here to add text]  
(i.e., number of cases required to achieve adequate statistical power or certainty of estimation)

Rationale for the sample size estimate: [Single-click here to add text]

Note: The rationale should include a clear explanation (or cited reference) for the method of sample size determination along with a statement of all assumptions required to perform that calculation so that an independent statistician would be able to reproduce the estimates from the information provided in the application.

Typically, a sample size estimate will require assumptions about the following:

- Anticipated distribution of marker values in the targeted population(s) (e.g., marker positivity rate if the marker is dichotomous)
- Assay success rates (based on anticipated rates of technical failures, degraded or insufficient biospecimens, etc.)
- Event rates or number of events anticipated for the cases included in the primary analysis
- Expected differences in outcomes or magnitudes of associations (e.g., hazard ratio or other “effect” size)

These assumptions and estimates need to be supported by preliminary data or previous studies that should be described either in this section or in the background section.

### **19. Statistical considerations for secondary objectives (if applicable)**

Detailed statistical considerations for addressing your secondary objectives are typically not required, but a general description of the intended approach (e.g., Cox proportional hazards regression modeling) should be provided.

However, if your secondary objectives involve very large numbers of analyses (e.g., examining association of expression of thousands of individual genes with a clinical endpoint) or will consume large amounts of biospecimens, please provide more detail to justify that the proposed analyses will be a productive use of the resource and not generate an unacceptably large number of spurious results.

Statistical considerations for secondary objectives (if applicable):  
[Single-click here to add text]

### **20. Projected start date:** [Single-click here to add text]

**21. Projected completion date:** [Single-click here to add text]

#### **DATA SHARING**

Research projects using biospecimens from NCTN clinical trials are subject to the requirements in NIH policies for data sharing and public access to publications, listed below, and to any applicable requirements of binding collaborative agreements.

Final NIH Statement on Sharing Research Data

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-03-032.html>

[http://grants.nih.gov/grants/policy/data\\_sharing/](http://grants.nih.gov/grants/policy/data_sharing/)

NIH Genomic Data Sharing Policy

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-124.html>

<http://gds.nih.gov/>

Revised Policy on Enhancing Public Access to Archived Publications Resulting from NIH-Funded Research

<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-033.html>

<http://publicaccess.nih.gov/index.htm>

If the biospecimens are from a trial that was conducted under a binding collaborative agreement with NCI or a pharmaceutical company (for example, with a company that supplied the drug), data sharing may have to await the timelines stipulated in those agreements. Studies conducted under a NCI/CTEP IND are subject to the terms of the CTEP IP Option ([http://ctep.cancer.gov/industryCollaborations2/guidelines\\_for\\_collaboration.htm](http://ctep.cancer.gov/industryCollaborations2/guidelines_for_collaboration.htm)) as well as the terms of the CTEP Collaborative Agreement under which the study is conducted. Similarly, studies conducted under a NCTN Group or Company IND will also be subject to the terms of the agreement between the Collaborators. Any discoveries from research performed on such specimens will be subject to the CTEP IP Option and/or the licensing terms as required by these agreements.

Approved proposals will also be subject to review and comment by the pharmaceutical Collaborator if the biospecimens are from a trial under a NCI/CTEP collaborative agreement.

**Please contact CTEP ([NCICTEPpubs@mail.nih.gov](mailto:NCICTEPpubs@mail.nih.gov)) prior to release of any data to a publicly available database.**

For trials under a collaborative agreement, you will also be required to send any abstracts and primary manuscript(s) resulting from your study to NCI ([NCICTEPpubs@mail.nih.gov](mailto:NCICTEPpubs@mail.nih.gov)) for review and Collaborator comment prior to submission (30 days prior for manuscripts, 3-7 days prior for abstracts).

#### **22. Data-sharing plan**

Please describe your data-sharing plan: [Single-click here to add text]

Note: Options for data sharing include submitting your data to the NCTN Data Archive (once your data are published), dbGaP, NCI Genomic Data Commons, GEO, SRA, the Cancer Genomics Hub, or other NIH-designated data repository. If you share your data via an NIH-designated data repository, you may also share your data via other, non-NIH-designated repositories.

### **23. Signature**

I acknowledge that my research projects using biospecimens from NCTN clinical trials are subject to the requirements in NIH policies for data sharing and public access to publications and to any applicable requirements of collaborative agreements.

Principal Investigator Name: \_\_\_\_\_

Signature: \_\_\_\_\_ (You may electronically sign.)

Date: \_\_\_\_\_

#### *REFERENCES*

Please provide your references here.

#### **APPENDICES**

You may provide further detail on your proposed correlative study as appendices to this form.

#### **REQUIRED ATTACHMENTS**

Please attach the following:

- Letters of collaboration from each co-investigator
- Any confirmation sent by the Group biobank about biospecimen and data availability