National Cancer Institute (NCI)
Experimental Therapeutics Clinical Trials Network (ETCTN) Guidance

# NCI Biomarker Review Committee

## Contents



## Introduction

### *Studies Requiring BRC Review*

The NCI Division of Cancer Treatment and Diagnosis (DCTD) Biomarker Review Committee (BRC) is responsible for reviewing the biomarker components of ETCTN clinical trials. Trials that are filed to NCI Cancer Therapy Evaluation Program (CTEP) INDs will require BRC review and approval if they meet any of the following criteria:

- Integral or integrated biomarkers (as defined below)
- CTEP funds are requested for sample collection and/or performance of the assay
- Requires mandatory biopsies
- Procedure is burdensome on the patient (invasiveness, schedule, etc.)

Laboratory correlatives that are generally not reviewed by BRC include pharmacokinetic assays, antidrug antibody assays, and flow cytometry of peripheral blood and bone marrow.

### *Timing of BRC Review*

The BRC review occurs in parallel with CTEP's Protocol Review Committee (PRC) review of the LOI and may continue as the study moves through protocol development and CTEP protocol approval. CTEP will not approve an LOI that includes integral biomarker assays until those assays have been approved by the BRC. Integrated markers may be reviewed by the BRC after the LOI approval has occurred, although the Protocol Chair must provide the information needed for BRC review and approval before a protocol may be submitted. In some instances, this stipulation may be waived by CTEP.

## Procedure

1) Prior to initial LOI submission, the Protocol Chair prepares assay information

a) Biomarker assay checklists and templates may be required as part of the LOI submission. The Protocol Chair should carefully review the instructions provided in the Correlatives section of the LOI form to determine what additional documentation is required for their LOI.
    i) Links to the checklists and templates can be found within the Correlative section of the LOI form.
b) CTEP encourages investigators to:
    i) Consult the "Guidelines for the Development and Incorporation of Biomarker Studies in early Clinical Trials of Novel Agents" (Dancey et al., CCR 16(6):1745-55, 2010) (doi: 10.1158/1078-0432.CCR-09-2167).
    ii) Discuss their biomarker plan with the Investigational Drug Branch (IDB) drug monitor before submitting an LOI

2) The BRC review of proposed integral assay(s) will occur in parallel with CTEP's PRC review of the LOI. The BRC review of proposed integrated assay(s) may occur at the time of LOI review or may take place after the protocol is submitted to CTEP.
3) Comments from the BRC reviewers will be incorporated into CTEP's LOI consensus review or may be provided as a separate set of review comments from the CTEP Protocol and Information Office (PIO).
4) The Protocol Chair will address each of the BRC comments and submit the response to the CTEP PIO.
5) The BRC approval or disapproval letter(s) will be provided to the Protocol Chair by the CTEP PIO and will specify the BRC review outcome for each of the proposed biomarker assays.
6) The Protocol Chair may need to update the biomarker assay plan within the protocol as a result of the BRC review. Any necessary updates must be submitted to CTEP in the form of a revision or amendment.

## Definitions

*The following definitions are from the July 5, 2016 NCI ETCTN Program Guidelines.*

An **investigational laboratory assay** is one that has not been cleared or approved by the FDA for the purpose for which it will be used in the trial.

An **integral biomarker** is one that is inherent to the design of the trial and must be measured in real-time for the trial to proceed. Briefly, markers are integral when they are essential for conducting the study as they define eligibility, stratification, disease monitoring or primary study endpoints. Any laboratory result that will be reported to the patient or his/her physician must be obtained in a CLIA-certified laboratory. An integral assay that will be used to determine eligibility or treatment may need to be performed under an Investigational Device Exemption (IDE) from the FDA.

Markers are considered **integrated** when they actually are testing a hypothesis based on preexisting data and not simply generating hypotheses. Such integrated markers need to be performed ideally on all patients in a trial and the assay should already have been tested on human specimens like those to be collected on the trial and demonstrated reproducible analytic qualities.

In contrast, **exploratory biomarkers** may not be performed on all subjects in a trial, and collection of these exploratory markers by investigators participating in the trial may be voluntary. Exploratory biomarkers will not undergo BRC review, except when NCI funds are requested for collection or for the marker analysis.

## Links

NCI Decision Tree for Determining the Need for LOI or Protocol Review by the BRC:
https://ctep.cancer.gov/protocolDevelopment/ancillary_correlatives.htm

Biomarker Review Guidelines:
https://ctep.cancer.gov/protocolDevelopment/ancillary_correlatives.htm

LOI Submission Form:
https://ctep.cancer.gov/protocolDevelopment/lois_concepts.htm