**Memorandum**

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**SUBJECT:** Guidelines for Biomarker Assays Used in CTEP-Sponsored, Early Phase Clinical Trials Performed Under CTEP IND

**TO:** Investigators and Company Collaborators

With the current emphasis on biomarker-driven drug development and the increasing inclusion of integral and integrated biomarkers in our trials, it is necessary to ensure that fit-for-purpose assays of these biomarkers are incorporated in CTEP-sponsored protocols. To that end, the NCI Division of Cancer Treatment and Diagnosis (DCTD) has formed the Biomarker Review Committee (BRC), which is now responsible for reviewing the biomarker components of CTEP-sponsored clinical trials. Specifically, Letters of Intent (LOIs) for trials that are not reviewed by an NCI disease-specific steering committee will require BRC review and approval if they include any of the following:

- integral and/or integrated markers

- requests for NCI funding for biomarker assays

- requests for NCI funding for sample acquisition

Exploratory biomarkers that will not be funded by NCI will not undergo BRC review.

Briefly, markers are integral when they are essential for conducting the study as they define eligibility, stratification, disease monitoring or study endpoints. 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 in human subjects with the disease in question 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. However, in some cases, the distinction between an integrated and exploratory biomarker may be difficult, and NCI may decide to review the biomarker in such cases. Additional information about the definitions of integral and integrated biomarkers can be found at the following NCI website: <http://www.cancer.gov/aboutnci/organization/ccct/funding/BIQSFP/2013-Updated-BIQSFP-Announcement>[[1]](#endnote-1).

To comply with OEWG timelines, BRC reviews will occur in parallel with CTEP’s Protocol Review Committee (PRC) and will be coordinated by the CTEP Protocol Information Office (PIO). Comments from the BRC reviewers will be incorporated into CTEP consensus reviews that will be sent to the investigators.

*Note: Because integral biomarkers are critical to carrying out the clinical trial, BRC approval of the integral biomarker is necessary prior to LOI approval.* Accordingly, CTEP strongly encourages investigators to include the assay information described below when submitting the LOI. In addition, investigators are encouraged to discuss their biomarker plan with the Investigational Drug Branch (IDB) drug monitor before submitting an LOI.

Integrated markers may be reviewed by the BRC after the LOI approval has occurred, although investigators must provide to PIO the information needed for BRC review and approval before a protocol may be submitted. The submission of information on integrated markers should be submitted as an amended LOI, where the integrated marker information is appended to the previously approved LOI.

When preparing a proposal which incorporates biomarkers, investigators should 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). When submitting the LOI, investigators should be certain to provide sufficient information about assay methodology and operating characteristics to allow BRC reviewers to make an adequate assessment. This will avoid delays in review of the LOI and will help to ensure compliance with Operational Efficiency Working Group (OEWG) timelines. To facilitate biomarker review, investigators should utilize the CTEP study checklist that is available on the CTEP website at <http://ctep.cancer.gov/protocolDevelopment/default.htm#ancillary_correlatives>.

Please note that failure to provide sufficient information to allow NCI reviewers to evaluate the assay may delay LOI or protocol approval.

1. Note (added Oct 2021): this link has been retired. Please visit the LOI Submission Form (<https://ctep.cancer.gov/protocolDevelopment/lois_concepts.htm>) for more information about the definitions of integral and integrated biomarkers. [↑](#endnote-ref-1)