

Biomarker, Imaging, & QOL Studies Funding Program (BIQSFP)

'16 Study Checklist for Clinical Trials with BIOMARKER ASSAYS for Treatment/Symptom Science /Supportive Care Studies

INSTRUCTIONS: For **INTEGRAL** assay, respond to Items 1-6, 8.
For **INTEGRATED** assay, respond to Items 1, 2, 4-8.

Please submit a response to each of the criteria below and complete one Study Checklist for **each** biomarker endpoint. The Proposal Package must also include a budget at the time of submission that clearly details the Direct and Indirect costs of the requested funding. The budget for the project should use the standard PHS 398 budget form (<http://grants.nih.gov/grants/funding/phs398/phs398.html>) along with a narrative justifying each requested cost. The Budget packet must include a completed NIH biosketch form for each study PI. Form SF424 can be found at: <http://grants.nih.gov/grants/funding/424/index.htm#format>. Additional information on the new biosketch requirements can be found at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-024.html>.

NOTE: INTEGRATED biomarker study applications must be submitted after parent concept approval but prior to protocol activation. Subsequent NCI prioritization and approval for funding will be decided by CTROC after evaluation of the INTEGRATED study(s) by the respective NCI Steering Committee (SSC).

1. For an integral or integrated assay, indicate the role(s) of the biomarker assay in the trial:
 - A. Eligibility criterion
 - B. Assignment to treatment
 - C. Stratification variable
 - D. Risk classifier or score
 - E. Other (describe in detail)
2. Identify the specific individual(s) and laboratory(ies) who are being considered for conducting the assay(s) for the trial.
3. Integral laboratory assays used for clinical decision-making must be performed in a CLIA-certified facility. Provide the lab's CLIA number that is performing the integral biomarker study(ies) and the expiration date of the certificate.
4. Describe the assay:
 - A. Specify the analyte(s), technical platform, and sources of assay components (e.g., reagents, chips, and calibrators).
 - B. Describe the specimens, and anticipated methods for specimen acquisition, fixation or stabilization and processing.
 - C. Describe the scoring procedures and type of data to be acquired
 - quantitative/ continuously distributed
 - semi-quantitative/ordered categorical
 - qualitative/non-ordered categorical
5. Provide data on the clinical utility of the integral/integrated assay as it will be used in the trial:
 - A. Provide background information that justifies the use of this assay result as a marker for this trial. For example, if the integral marker will be used as a stratification or treatment-

determining variable, data supporting its prognostic or predictive association with a main trial endpoint should be described or referenced.

Note: If the trial objectives include an evaluation of the association of the integral marker with a new clinical endpoint or factor not previously studied, the statistical section of the concept should explain how the magnitude of the association or effect will be measured and provide power calculations for any statistical tests that are planned.

- B. Describe the expected distribution of the biomarker in the study population.
 - C. If cutpoints will be used, specify the cutpoint(s) and describe how these will be used in the trial). Provide the rationale for the cutpoint(s) selected. What proportion of subjects is expected to have values above and below the proposed assay value cutpoints? What magnitude of effect (e.g., treatment benefit) or outcome (e.g., prognosis) is expected for patients with assay results above and below the proposed cutpoint(s)?
 - D. Describe under what conditions treating physicians and or patients will be able to access the biomarker assay results.
6. Provide data on the analytical performance of the assay.
- A. For *in vitro* tests, describe the current status of studies defining the accuracy, precision, reportable range, reference ranges/intervals (normal values), and failure rate of the assay as it is to be performed in the trial (e.g., performance of test on specimens intended to be used in the clinical trial). Describe the use of positive and negative controls, calibrators, and reference standards for clinical assays. Describe any critical preanalytic variables. For guidance on regulatory requirements for laboratory assays please visit: http://www.cms.gov/CLIA/05_CLIA_Brochures.asp. Applicants are encouraged to submit a laboratory Standard Operating Procedure (SOP) as an appendix, to support validation of the assay(s) being proposed.
 - B. If the assay will be performed at more than one site, describe how inter-laboratory variability in the measurements listed in 5A above will be assessed. Describe how these sources of variation will be minimized to maintain performance at all sites within acceptable limits and to prevent drift or bias in assay.
 - C. Provide turn-around-time for reporting assay results to the clinical PI (for INTEGRAL studies).
7. For an **INTEGRATED** study, provide justification for the assay to be completed in real time (if applicable).
8. The Budget Justification should include a description of potential cost-sharing approaches for the assay (e.g., billing to third-party payers, partial funding from commercial partners, choosing between academic vs. commercial labs, etc.) along with justification for the costs of academic vs. commercial laboratories.

8/08,3/09,3/10,3/11,3/12,4/13,11/13,12/14,12/15

**Please complete and return to the appropriate CTEP/DCP
PIO and Dr. Raymond Petryshyn at CCCT
(petryshr@mail.nih.gov).**

Thank you.