

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

**Study Checklist for Large Randomized Phase 2 and Any Phase 3 Trials with Biomarker Assays / Imaging Tests**

**INSTRUCTIONS:** For **INTEGRAL** assay/test, respond to Items 1-5.  
For **INTEGRATED** assay/test, respond to Items 4-5 and 6b.

**Please submit a response to each of the criteria below and complete one Study Checklist and the BIQSFP Cost Estimate Worksheet for each Biomarker and/or Imaging endpoint.**

1. For an integral or integrated assay, indicate the role(s) of the biomarker assay or imaging test 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) or imaging departments who are being considered for conducting the assay(s) or imaging test(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 or imaging test:
  - A. Specify the analyte(s), technical platform, and sources of assay components (e.g., reagents, chips, and calibrators), imaging devices or imaging agents.
  - B. Describe the specimens, and anticipated methods for specimen acquisition, fixation or stabilization and processing. For imaging tests, describe any patient preparation procedures, as well as the procedures for imaging, analysis and interpretation of the results.
  - C. Describe the scoring procedures and type of data to be acquired
    - quantitative/ continuously distributed
    - semi-quantitative/ordered categorical
    - qualitative/non-ordered categorical
  - D. If cutpoints will be used, specify the cutpoint(s) and describe how these will be used in the trial (also, see 4C above).
5. Provide data on the clinical utility of the integral/integrated assay or imaging test as it will be used in the trial:
  - A. Provide background information that justifies the use of this assay or imaging test 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, provide the rationale for the cutpoint(s) selected. What proportion of subjects is expected to have values above and below the proposed assay or imaging test value cutpoints? What magnitude of effect (e.g., treatment benefit) or outcome (e.g., prognosis) is expected for patients with assay or imaging test 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/imaging test results.
6. Provide data on the analytical performance of the assay or imaging test.
- A. For *in vitro* tests, describe the current status of studies defining the accuracy, precision, reportable range, reference ranges/intervals (normal values), turn-around time and failure rate of the assay as it is to be performed in the trial. For imaging tests, describe what performance characteristics are known. State and justify the limits of acceptable performance. Describe the use of positive and negative controls, calibrators, and reference standards for either imaging or 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](http://www.cms.gov/CLIA/05_CLIA_Brochures.asp) .
  - B. If the assay or imaging test 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 or imaging test results.