BIQSFP BIOMARKER EVALUATION TEMPLATE

Evaluator's Name:

Date of Evaluation:

Concept/BIQSFP ID Number and Title:

Instructions for BIQSFP Biomarker Evaluators: Please complete one (1) Evaluation Template for each biomarker study. There could be more than one BIQSFP application (i.e., multiple biomarkers, or biomarker and imaging) associated with a single clinical trial, and each should be submitted on a separate BIQSFP form.

Your responsibilities consist of evaluating the biomarker and assay performance and validation aspects of the proposed study by providing written comments on this form in response to the specific questions that follow the evaluation criteria below.

Please use the attached *BIQSFP Proposal Package* in completing your evaluation. After completing this form, please save it to a new file, attach the form to an e-mail message referencing the concept/BIQSFP number, and forward the email to the CTEP, DCP, CCCT, or EMMES Program Staff who requested this evaluation from you. Submit your response at least 1 week preceding the study evaluation conference call/meeting, so that all perspectives may be shared, and your written comments viewed by other evaluators of this study. You will likewise be provided access to the written comments of the other evaluators.

Key evaluation criteria:

A. Whether the study is integral or integrated

Based on the definitions provided below, evaluators should assess whether the proposed study is *integral* or *integrated*. Integral studies have highest priority for BIQSFP funding. Studies that are neither integral nor integrated (e.g., exploratory studies) are not eligible for BIQSFP funding.

Integral Studies – Defined as assays/tests that must be performed in order for the trial to proceed or to support the primary analysis. Integral studies are inherent to the design of the trial and must be performed on all participants, usually in real-time. The assay/test must support one of the trial's primary hypotheses. Integral studies have the highest funding priority.

Integrated Studies – These are intended to validate markers, imaging tests, or QOL/PRO instruments for possible use as an integral marker in future trials or in clinical practice. Integrated studies should test a specific hypothesis with a preplanned statistical design and are not hypothesis-generating or exploratory. Integrated studies must be

included in the protocol as a secondary objective. Integrated studies may require the assays/tests to be conducted real time during the trial or may be performed non-real time on samples that were collected during the course of the trial and then stored for testing and analysis at a later time.

B. Specification of assay procedure

For BOTH integral and integrated studies, evaluators should assess whether the assay or imaging test has been specified in sufficient detail in the BIQSFP documents. For biomarker assays, this specification should include preanalytical requirements for specimen collection, description of the technical protocol, reagents, positive and negative controls, scoring methods, and cutpoints, as applicable.

C. Adequacy of information provided about the analytical (technical) performance of the assay procedure

Evaluators are requested to provide comments about whether sufficient documentation of acceptable analytical (technical) performance has been provided. The BIQSFP documents should provide information about accuracy, precision, reportable range, reference ranges/intervals (normal values), limit of detection, limit of quantification, and failure rate of the assay/test, as applicable, and in the context of how the procedure is to be performed in the trial (e.g., performance of test on the types of specimens or patients expected in the clinical trial and/or whether the specimens will be batched for analysis or analyzed in real-time).

The evaluators should consider whether performance metrics have been clearly defined and sufficient information has been provided about the numbers and types of specimens (or subjects) involved in the analytical (technical) performance studies. Details should include the distribution of biomarker or imaging measurements in the specimens or subjects studied in the performance assessment (e.g., how many were positive versus negative for the biomarker) and descriptions of the replication schemes used for precision and reproducibility evaluations.

The above information is necessary for proper interpretation of the reported analytical (technical) performance results. The requirement for information on analytical performance also applies to a commercially-available assay/test. Regardless of whether a biomarker assay is a laboratory developed test or is a commercially available kit, the analytical performance study description should provide supporting data to establish that the test performance has been evaluated in the laboratory that will be performing the assay for the clinical trial, and according to the same technical protocol (including specimen preanalytical factors).

D. Pre-specified hypotheses, intended role, and supporting data

Pre-specified hypotheses and aims and a clear intended role for the biomarker measurement in disease management, with supporting data from prior studies, should be provided in the BIQSFP documents. Evaluators should comment on the robustness of the preliminary or supporting data, considering factors such as the design and analysis of the studies that generated those data. The supporting data need to be of sufficient

strength and quality to justify the proposed investigation of the assay/test in an integrated study or its proposed use in the execution of the parent concept (integral assay/test). For integral assays/tests that are an inherent part of the trial design (e.g., only patients whose tumors overexpress the integral protein biomarker are eligible for entry into the trial and for randomization to treatment), the biomarker or imaging hypothesis is intimately tied with the treatment question and will have been reviewed already as part of the review of the treatment objectives of the parent clinical trial. However, if the evaluators have any concerns about the adequacy of the background data supporting the use of the biomarker in the proposed manner, they are encouraged to comment.

If the BIQSFP study involves a comparison of assays/tests, a data analysis plan should be provided which describes how assay/test superiority will be determined.

Evaluator Comments:

1. Based on the definitions provided under evaluation criterion A and on your evaluation of the objectives of the BIQSFP study, would you categorize this study as INTEGRAL, REAL TIME INTEGRATED, NON-REAL TIME INTEGRATED or EXPLORATORY? Please provide a brief explanation for your answer.

2. Is the assay procedure sufficiently described (see evaluation criterion B) to enable meaningful, well-defined, and interpretable quantifications of the biomarker?

   Strengths:
   Weaknesses:

3. Is the analytical or technical performance of the measurement procedure (e.g., specificity, sensitivity, reliability, accuracy, reproducibility, as applicable) well-documented in the BIQSFP proposal (see evaluation criterion C), and does it meet sufficiently high-performance standards fit for use in the study?

   Strengths:
   Weaknesses:

4. Is the underlying scientific objective of the assay/test well-defined, feasible, and achievable? Are the underlying scientific questions and hypotheses clearly stated and supported by preliminary data and results from previous studies?

   Strengths:
   Weaknesses:

5. Are there any concerns regarding feasibility and logistics associated with aspects such as quality specimen acquisition and processing, timing of measurements,

turnaround time, and return of results in time for therapy administration? Please comment on whether the assay is "fit-for-purpose" within the context of this trial.

Strengths:
Weaknesses:

6. Comment on the feasibility of standardizing or harmonizing this test across different clinical laboratories in the future to yield consistent results and interpretations that can guide decision-making. What is the potential of the test to change clinical practice and improve patient care?

   Strengths:
   Weaknesses:

7. Based on the strength of the information presented and your scientific judgment, please indicate your level of enthusiasm for the study:

High				**Mild**
1	2	3	4	5

SCORE: _____

8. Please comment on the attached Budget and Justification. Provide recommendations if needed. Are there potential cost-sharing approaches that can be developed with entities that would eventually commercialize the test?

It is understood that by agreeing to assist in this evaluation, you have no conflicts of interest with this concept. In addition, all unpublished information, reports, and discussions are strictly confidential.