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 (e.g., multiple biomarkers, imaging, symptom science/QOL) associated with a single clinical trial, and each should be submitted on a separate BIQSFP form.

Your responsibilities consist of evaluating the biomarker, 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, real time integrated, non-real time integrated, or exploratory

Based on the definitions provided below, evaluators should assess whether the proposed study is *integral*, *real time integrated*, *non-real time integrated*, or *exploratory*. Integral studies have highest priority for BIQSFP funding. Exploratory studies are not eligible for BIQSFP funding.

Integral Studies are 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.

Integrated Studies are intended to clinically validate markers, imaging tests or tools, or symptom science/QOL 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 (please see the definition of "exploratory" below). The assays/tests need to have already been analytically validated. Integrated studies must be included in

the protocol as secondary outcomes.

Real Time (RT) Integrated Studies need the assays or tests, including imaging scans, to be performed and/or assessed in real time during the trial. Real time studies may also involve special sample collection or processing and cannot be stored and batched for analysis later.
Non-Real Time (NRT) Integrated Studies do not require real time processing or testing of specimens. For example, NRT integrated assays/tests can be performed at a later time on patient scans or specimens collected as part of the clinical trial, and the results are not needed for trial eligibility, stratification, or treatment assignment.

Exploratory studies include studies characterizing physiological processes or molecular pathways to suggest new therapeutic approaches that might be worthy of further investigation. Studies are also considered exploratory when they aim to test preliminary hypotheses or to further refine such hypotheses in situations where background data in the specific disease type or therapeutic context are limited.

B. Specification of assay procedure

For BOTH integral and integrated studies, evaluators should assess whether the assay 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 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. Regardless of whether a biomarker assay is a laboratory developed assay 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 in an integrated study or its proposed use in the execution of the parent concept (integral assay).

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 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, a data analysis plan should be provided which describes how assay 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), and will the test yield meaningful, well-defined, and interpretable quantifications of the biomarker that will guide decision-making?

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?

   Strengths:
   Weaknesses:

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

   Strengths:
   Weaknesses:

5. Are there any concerns regarding feasibility and logistics associated with quality specimen acquisition and processing or image acquisition, timing of measurements, turnaround time for testing and/or analysis, 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. What is the potential of the test to change clinical practice and improve patient care?

   Strengths:
   Weaknesses:

7. 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 extent of standardization of the assays/tests/tools as to be transferable to the non-research setting?

   Strengths:
   Weaknesses:

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

High				**Low**
1	2	3	4	5

SCORE: _____

9. 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?

10. Please list any KEY QUESTIONS that the study Principal Investigator could address, which might change your recommendation regarding the BIQSFP proposal.

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.