IMAGING EVALUATION TEMPLATE

Evaluator's Name:

Date of Evaluation:

Concept/BIQSFP ID Number and Title:

Instructions for BIQSFP Imaging Evaluators: Please complete one (1) Evaluation Template for each imaging 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 imaging, test 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 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 imaging tests or tools for possible use in an integral study 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 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 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 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 to develop novel imaging tests to suggest new therapeutic or diagnostic approaches or application to diseases 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 imaging procedure

For BOTH integral and integrated studies, evaluators should assess whether the test has been specified in sufficient detail in the BIQSFP documents. For imaging tests, this specification should include preanalytical requirements for test completion, site credentialing, positive and negative controls, scoring methods, and cut points, as applicable. The study application should delineate the magnitude of effect (e.g., treatment benefit) or outcome (e.g., prognosis) expected for patients with imaging results above and below the proposed cutpoint(s).

Mechanisms for assessing inter-facility variability in the measurements along with the analysis tool to manages inter-site variability should be noted. How will these sources of variation will be minimized to maintain performance at all sites within acceptable limits and to prevent drift or bias in imaging test results or analysis?

C. Adequacy of information provided about the analytical (technical) performance of the test 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 ranges of interpretation, reference ranges/intervals (normal values), limits of quantification, and failure rate of the test, as applicable, and in the context of how the procedure is to be performed in the trial (e.g., performance of the test on the patients and/or whether the tests 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 tests (or subjects) involved in the analytical (technical) performance studies. Details should include the distribution of imaging test measurements in subjects studied in the performance assessment (e.g., how many were positive versus negative for the

imaging) and descriptions of the replication schemes used for precision and reproducibility evaluations. If the integral imaging test or analysis result 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.

Test scoring procedures and type of data to be acquired, such as quantitative/ continuously distributed, semi-quantitative/ordered categorical, or qualitative/non-ordered categorical is adequately described in the study application.

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 standard/commercially available tests. If preclinical validation of the imaging test is site-specific, the analytical performance description should provide supporting data such that the technical protocol is available and easily transferable to other sites, as applicable.

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

Pre-specified hypotheses and aims and a clear intended role for the imaging 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 test in an integrated study or its proposed use in the execution of the parent concept (integral test).

For integral tests that are an inherent part of the trial design, the imaging hypothesis is intimately tied with the treatment or response 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 imaging test in the proposed manner, they are encouraged to comment.

If the BIQSFP study involves a comparison of imaging tests, a data analysis plan should be provided which describes how imaging 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 testing procedure sufficiently described (see evaluation criterion B), and will the test yield meaningful, well-defined, and interpretable test results that will guide decision-making?

   Strengths:
   Weaknesses:

3. Is the analytical or technical performance of the test procedure and analysis (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. 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 test well-defined, feasible, and achievable?

   Strengths:
   Weaknesses:

5. Are there any concerns regarding feasibility and logistics associated with quality imaging acquisition and processing, timing of measurements, turnaround time for testing, analysis, and/or results reporting in time for therapy administration (as applicable)? Please comment on whether the test 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 sites in the future to yield consistent results and interpretations that can guide decision-making. What is the extent of standardization of the proposed test 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.