QOL Study Evaluation Guidelines

Quality of Life Studies (QOL) Funding Program

Purpose and Background

As part of its Prioritization and Scientific Quality Initiatives, the Clinical Trials Working Group (CTWG) of NCI recommended establishing a funding mechanism and prioritization process for essential correlative QOL studies that are incorporated into the fundamental design of a clinical trial. The objective of this initiative is to ensure that the most important quality of life studies can be initiated in a timely manner in association with clinical trials.

Quality of life studies embedded in clinical trials often lead to scientific observations that validate targets, reduce morbidity, predict treatment effectiveness, facilitate better drug design, identify populations that may better benefit from treatment, improve accrual and retention, and ultimately lead to change in the standard of practice. Support for timely and important studies during the clinical trial concept development phase will ensure timely development of effective, informative and high impact clinical trials.

The primary purpose of this funding mechanism is to support quality of life studies that are integral to and/or integrated with phase 3 clinical treatment trials conducted by the Cooperative Groups (CG's) and Community Cancer Oncology Program (CCOP) Research Bases.

Quality of Life Studies

QOL studies can be integral or integrated tests, assays, and/or tools. They must be part of the clinical trial design from the beginning (assessments conducted while the trial is open). They are intended to inform on treatment options and side effects by validating the biological and functional clinical correlates of patient–reported outcome (PRO) data. These may also include biomarker assays and imaging tests that may be used for decision making in future trials.

Currently, DCP funds quality of life studies that obtain information for use in patient-physician decision making that help the patient prepare for and interpret the treatment experience. Examples of this DCP support may include studies where differences between treatments in survival or other disease-related endpoints are expected to be minimal or when treatment arms represent very different treatment scenarios. Assessments may include, but are not limited to, qualitative data, toxicity impact, convenience, psychosocial outcomes and function.

BIQSFP proposals for funding of **INTEGRAL** QOL studies must be submitted concurrently with the parent concept. **INTEGRATED** QOL study applications **must be submitted after parent concept approval and must be received within four months (16 weeks)** of notification of parent concept approval.

Eligible categories of quality of life studies and examples include:

- QOL studies to obtain additional information for use in patient–physician decision making or to help the patient prepare for and interpret the treatment experience when the collection of QOL data requires resources beyond the usual cancer control credits or per case reimbursement.
- Studies that validate measures previously tested in smaller studies. QOL measures that have been piloted in smaller studies and are supported by preliminary data require

full validation in a phase 3 trial. This includes evaluating patient reported outcomes (PRO) as complementary adjuncts to clinician-assessed outcomes for measuring toxicity (e.g., adverse events as measured by Common Toxicity Criteria).

- Studies in the PRO measurement field with the integration of modern measurement theory for the development of brief, precise, and valid PRO measures. These advancements provide an examination of the benefits of integrating these measures, including electronic data capture, into clinical trials. Examples of studies that fall into this category may include: computer-based testing, experience sampling, and multiple brief symptom assessment (as opposed to infrequent and lengthier assessment).

There is growing interest in the role of objective measures such as biomarkers, imaging studies, and measures of activity such as pedometers and actigraphs that can further inform symptoms, QOL assessments, and selected measures that validate PRO data such as:

- Studies that provide "objective" correlates to self-report measures that are not easily supported through funding for clinical trials. Concurrent collection of an "objective" test along with a performance measure provides stronger data when following patients on a symptom management or quality of life trial. Examples of studies in this category may include: enhancing measures that validate patient self-report of fatigue or physical function with objective actigraphy; and neuropsychological testing in studies of cognitive effects from therapy, or in following patients with brain tumors or metastases.
- Studies that are "predictive" measures with testable hypothesis(es) and a high likelihood to give validated interpretations, and correlative measures to predict morbidity, safety, pathophysiologic mechanisms of symptom expression, and/or treatment efficacy and genetic determinates of symptom expression, quality of life endpoints and treatment efficacy. Examples of these study measurements may include: cytochrome P450 metabolism; cytokine analyses; pharmacokinetic studies for drug interactions; neuroendocrine studies, and fMRI for cognitive changes.

Criteria for Review and Prioritization of QOL Studies

Prioritization and evaluation criteria include:

- The potential to impact patient morbidity or quality of life with clinically meaningful benefit.
- The potential to move science forward in cancer related quality of life by adding critical knowledge.
- The strength of the preliminary data supporting the hypothesis(es) to be tested and methods proposed.
- A clearly defined process for data and specimen collection.
- A statistical plan with adequate power for the quality of life correlative study hypothesis(es).
- Measures that are reliable, valid and appropriate to the population of interest.
- Feasibility of proposal such that completion can be accomplished efficiently and in a reasonable time frame.

Each category is of equal priority, however in general, higher consideration is placed on studies that are scientifically grounded and well developed, use well validated and reliable measures, and are likely to have the largest impact on clinical practice.

It is not intended that any priority or particular level of merit be assigned to one of the previous criterions over another. Based on the strength of the information presented and your scientific judgment, you will be asked to rate your level of enthusiasm for the study on a five-point scale from High to Mild.

BIQSFP submission should include a completed Study Checklist for each quality of life component. The elements in the Study Checklist are listed below. The application should include a response to these elements.

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

'14 Study Checklist for Randomized Phase 3 Trials with Quality of Life (QOL) Components

INSTRUCTIONS: Please submit a response to each of the criteria below. Please complete one Study Checklist and the Form PHS 398 Grant Budget Worksheets for each QOL endpoint.

NOTE: One-time INTEGRATED QOL study applications must be submitted after parent concept approval and must be received within four months (16 weeks) of notification of parent concept approval. Subsequent NCI prioritization and approval for funding will be decided by CTROC after evaluation of the INTEGRATED study(s) by the respective SSC.

1. State the HRQOL (health-related quality of life) hypothesis(es) and its scientific foundation. Specify the study endpoint(s).

2. Identify the HRQOL instrument(s) to be used to test each hypothesis, the basis for choosing each instrument, and the timing of the assessments.

3. For each instrument, document its validity, reliability, and responsiveness in the selected patient population. Specify the minimum important difference (MID) or metric for clinically-significant change.

4. For each instrument, identify whether it is INTEGRAL or INTEGRATED.

5. Describe any included *objective* correlates that enhance the patient-reported outcomes data (e.g. actigraphy, imaging, pulse ox, etc).

6. Identify any *biomarker or imaging* correlates of the patient-reported outcome measure(s) that will be collected (e.g., molecular, protein, other assays or tests).

7. Explain how patient non-compliance, missing data and/or early death may impact the analysis.

8. How will visually-challenged, non-English speaking patients be accommodated when completing the instrument(s)?

9. Describe the procedures for data collection and data monitoring including the training of data collection personnel.

3/09,3/10,3/11,3/12,11/13

Please complete the attached QOL STUDY EVALUATION TEMPLATE.

Thank you.