

## QOL/PRO Study Evaluation Guidelines

### Quality of Life / Patient-Reported Outcomes Studies (QOL/PRO) 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.

QOL/PRO 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 QOL/PRO studies that are integral to and/or integrated with clinical treatment trials conducted by NCI National Clinical Trials Network (NCTN) groups and NCI Community Oncology Research Program (NCORP).

#### Quality of Life Studies

**QOL/PRO studies can be integral or integrated** assays, tests, and/or instruments. Assays may include biomarkers, imaging tests, or PROs. 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 biological and functional clinical correlates.

Currently, DCP funds QOL/PRO components in disease treatment trials 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.

**Integrated** QOL/PRO study applications must be submitted after parent concept approval but prior to protocol activation. Subsequent NCI prioritization and approval for funding will be decided by CTROC after evaluation of the QOL/PRO study by DCP and the respective NCI Steering Committee (SC), if applicable.

#### Eligible categories of quality of life studies and examples include:

- Studies that are adequately-powered and test specific biological and translational hypotheses.
- Studies that assess complex biological and physiological variables utilizing state-of-the-art measures to assess endpoints.
- 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 data requires resources beyond the usual cancer control credits or per case reimbursement.

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- Studies that validate measures previously tested in smaller studies. QOL/PRO/symptom science/supportive care measures that have been piloted in smaller studies and are supported by preliminary data require full validation in larger, more definitive randomized clinical trials.

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

- 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 science/supportive care or disease treatment trial. Examples of studies in this category may include: enhancing measures that validate patient self-report of fatigue or physical function with objective actigraphy; 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/PRO Studies**

Prioritization and evaluation criteria include:

- The potential to impact patient morbidity and quality of life with clinically meaningful benefit.
- The potential to move science forward in cancer related symptom science/supportive care 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 testing the QOL/PRO correlative study hypothesis(es).
- Measures that are reliable, valid, and appropriate to the population of interest.
- Feasibility of the 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 QOL/PRO 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)***

**'16 Study Checklist for Clinical Trials with QOL/PRO Components**

**INSTRUCTIONS:** Please submit a response to each of the criteria below and complete one Study Checklist for each QOL/PRO endpoint. The Proposal Package must also include a budget at the time of submission that clearly details the Direct and Indirect costs of the requested funding. The budget for the project should use the standard PHS 398 budget form (<http://grants.nih.gov/grants/funding/phs398/phs398.html>) along with a narrative justifying each requested cost. The Budget packet must include a completed NIH biosketch form for each study PI. Form SF424 can be found at: <http://grants.nih.gov/grants/funding/424/index.htm#format>. Additional information on the new biosketch requirements can be found at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-024.html>.

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1. State the symptom science/QOL/PRO hypothesis(es) and its scientific foundation. Specify the study endpoint(s).
2. Identify the QOL/PRO 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. Applicants are encouraged to submit a symptom science/QOL/PRO Standard Operating Procedure (SOP) as an appendix, to support validation of the test/tool/instrument(s) being proposed.
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.
10. Provide turn-around-time for reporting instrument results to clinical PI (for INTEGRAL studies).

3/09,3/10,3/11,3/12,11/13,12/14,12/15

**Please complete and return the attached QOL/PRO STUDY EVALUATION TEMPLATE. Thank you.**