

SYSTEMATIC TREATMENT ENHANCEMENT PROGRAM – BIPOLAR DISORDER

SCIENTIFIC ADVISORY BOARD

ANCILLARY STUDY APPLICATION GUIDELINES

OVERVIEW

The Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) is a multicenter longitudinal (5-8 year) NIMH sponsored contract. The purpose of the this study is to improve the treatment of bipolar disorder utilizing a public health model to study treatment effectiveness for an inclusive sample of bipolar patients from a variety of clinical, ethnic and geographic subgroups. The methodology of Model Practice Procedures provides a common intervention model that can be implemented across many diverse treatment centers and provides answers to an array of important basic clinical outcome questions as well as quality of life and economic outcomes.

In addition, the coordinated network of treatment centers will provide a national resource for independent investigators. This will allow investigators to apply to NIMH for funding to conduct ancillary studies in innovative treatment areas as funding permits.

The Clinical Coordinating Center at MGH has established a network of at least 12 research treatment centers in which some 5,000 patients will be treated by 75-100 specially trained psychiatrists and 15-20 clinical specialists. Additional centers will participate as “Affiliated” sites (Standard Care Pathways only). Practitioners at all sites will use identical assessment procedures and implement therapeutic interventions, as called for by treatment guidelines (Model Practice Procedures), which integrate pharmacological and psychosocial interventions. Participating treatment centers will use this set of common assessment methods across Standard Care Pathways (SCP) and Randomized Care Pathways (RCP).

In the Standard Care Pathways, in which all treatment is open, treating psychiatrists will be trained to use clinical practice guidelines. These treatment choices will be applied at various decision points based on doctor-patient preference. In the Randomized Care Pathways treatment at key decision points is selected by randomization and is carried out under double-blind and open-label conditions.

ANCILLARY STUDY GOALS

The goals of the Ancillary Studies section of STEP-BD are to promote innovative lines of scientific inquiry regarding the understanding and treatment of bipolar disorder. The role of the STEP-BD Scientific Review Board is to determine scientific merit and compatibility of the ancillary study proposal in conjunction with the STEP-BD goals. Projects meeting these requirements will be certified as ancillary studies in a formal letter from the SAB. This certification can be used by the Principal Investigator in the application for funds from NIMH or other governmental funding agencies, foundations, or industry. Please note that this certification indicates that the investigator may go forward, with the SAB certification, to obtain funding. This certification does not guarantee that the ancillary study, following funding approval, will necessarily become part of the STEP-BD program. The ancillary study may have incurred significant time delays or design changes. It is anticipated that STEP-BD project needs and goals will change over time. For example, if there are two research projects studying the same innovative treatment, and one of ancillary studies is able to begin at an earlier date, that in all likelihood reduces or obviates the need for the other study.

ANCILLARY STUDY FUNDING

Funds are not directly available from STEP-BD. The scientific advisory board will evaluate all ancillary study proposals to determine their compatibility and consistency with the objectives of STEP-BD. The Applicant will be solely responsible to pursue these funding resources.

ELIGIBILITY FOR ANCILLARY STUDIES

Ancillary studies can be proposed by any investigator; eligibility is not limited to those participating in STEP-BD. Priority will be given to small, hypothesis-driven, single-site studies proposed by new or relatively inexperienced investigators as part of mentored research career development awards or other investigator-initiated mechanisms. Proposals for larger, multi-site studies will be considered only if the coordination of resources is directly addressed.

GUIDELINES FOR ANCILLARY STUDY APPLICATIONS

The following guidelines are to be used to prepare an application for the STEP-BD Scientific Advisory Board. To provide a uniform system of review and to assure that all proposals will be evaluated carefully and fairly, applicants must adhere to the following guidelines:

- I. The proposal should be easily read and understood by individuals who may not be experts in the specific area of research, but who are sufficiently knowledgeable in scientific areas related to the research to be able to evaluate the proposal in a fair manner.

- II. The proposal should follow the format outlined below:
 1. Cover Page naming all Investigators and Protocol Title
 2. Abstract
 3. Budget and Budget Justification; Curriculum Vitae (for PI only) and Biographical Sketch (for all other Investigators); and Other Support for all Investigators.
 4. STEP-BD Resources Required (e.g., data management, clinical monitoring)
 5. Proposal
 - A. Specific Aims
 - B. Background and Significance
 - C. Preliminary Studies (if applicable)
 - D. Research Design and Methods (including biostatistical design and analysis and gender and minority inclusion statement)
 - E. Human Subjects (including Subject population; Sources of research material; Recruitment and consent procedures; Potential risks; Risk management procedures; and Evaluation of risk/benefit ratio)
 - F. Vertebrate Animals (if applicable)
 - G. Literature Cited

Please note that sections A - D must not exceed 5 pages. Appendices should be limited. Please deliver twelve copies and an IBM-compatible diskette to the address below by 5:00 p.m. on the deadline date.

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REVIEW CRITERIA

Proposals will be evaluated according to their scientific merit, technical feasibility, additional burden placed on subjects or facilities participating in STEP-BD, and their potential for enhancing the overall impact of this initiative. Proposals that interfere with the main objective of the trial, divert resources from the study, adversely affect subject and site availability or participation, or compromise the public image of the initiative will not be approved.

REVIEW PROCEDURES

Submitted proposals are initially reviewed by the Chairperson of the STEP-BD Scientific Advisory Board to determine whether research content and direction meet established criteria and STEP-BD goals. At least two members of the STEP-BD Scientific Advisory Board are assigned by the Chairperson to act as primary reviewers and evaluate each proposal in a detailed manner. In addition, the Chairperson may ask other individuals to assist in reviewing applications on an ad-hoc basis. Each proposal is also reviewed by two outside reviewers (academicians with no relationship to the funding center who are selected from the scientific community) and the Government Project Officer. A copy of each application is sent to all members of the Committee. Those Committee members not designated as primary reviewers are encouraged to read the application and participate in the final determination.

If the proposal is approved, each voting member of the committee rates the proposal using current NIH numerical rating guidelines. The ballots are collected and tabulated by the Chairperson. The SA Board's decision and recommendations are forwarded to the Principal Investigator. If the proposal is approved, the Applicant will be able to use this certification in the formal application for funding. If the proposal is disapproved or deferred, the applicant receives a detailed explanation of the SA Board's decision from the Chairperson. If deferred, the application can receive a regular or expedited re-review. A proposal granted a deferral with regular review should be re-submitted with changes following guidelines for the initial submission and will be reviewed by the committee at the next scheduled meeting. A proposal granted a deferral with expedited review should be re-submitted following directions enumerated in a letter to the investigator from the Chairperson. In this case, the applicant should submit a detailed letter responding to the critique of the committee. The re-submission will be voted upon by the primary and outside reviewers by paper ballot without discussion at a meeting. A proposal receiving disapproval cannot be re-submitted to the Committee.

Applications will be accepted at any time. The Committee will be convened (in person or by conference call) every other month (odd months, e.g., January, March and so on) if there are pending applications. **Applications must be submitted at least five weeks prior to a scheduled meeting.** Applications submitted less than five weeks prior to a scheduled meeting will be deferred until the next meeting. A schedule of deadlines and meeting dates is available from STEP-BD.

REPORTING

The PI of ancillary study must submit an annual progress report to the SAB. This report can be a duplicate of the one submitted to the funding agency and should describe progress, difficulties, and future directions for the research. Publications developed from an ancillary study must include acknowledgement that the study is an ancillary study of STEP-BD.