INSTRUCTIONS FOR PREPARATION OF R34 CRITIQUES

National Institutes of Diabetes and Digestive and Kidney Diseases

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In your written review, you should comment on the following aspects of the application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals.

Please bring a double-spaced print copy of the reviews assigned to you to the meeting. In addition, bring your critiques on a disc if you have not e-mailed them or uploaded them into the Internet-Assisted Review system. This will facilitate the writing of the summary statements. Note: Your written reviews should not bear personal identifiers since comments will be minimally edited before being sent to the investigator.

EVALUATION OF R34 APPLICATIONS

PRIMARY REVIEWERS should provide an overall evaluation, briefly summarize the most important points of your critique, weighting the review criteria as you feel appropriate, and evaluating the overall impact of the research on the field. (Note: an application does not need to be strong in all categories to be judged likely to have a major scientific impact and thus deserve a high merit rating.) A description, which should be taken from the abstract of the application, is optional. In the critique, the five review criteria should be addressed as separate sections. If this is an amended application, address progress, changes, and responses to the critique from the previous review, indicating whether the application is improved, the same as, or worse than the previous submission. However, you are not constrained to address only the points identified in the previous review. These comments on progress and responsiveness to previous critiques should be provided either in a separate paragraph and/or under the appropriate criteria.

SECONDARY REVIEWERS need only prepare written critiques addressing the five criteria and recommendations, although comments on any other sections are welcome.

READERS should have read the assignment carefully and be conversant with it but are not required to supply a written critique, although it is appreciated.

1. **Significance:** Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge be advanced? What will be the effect of these studies on the concepts or methods that drive this field?

2. **Approach:** Are the conceptual framework, design (including the composition of the study population), methods, and analyses adequately developed, well-integrated, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

Preliminary data are not required for an R34 application. Studies submitted to this program should focus on developing preliminary data of feasibility of a proposed approach, or other information needed for the development and assessment of an application for a full-scale trial.

The rationale for the future large-scale intervention should be clearly described. Applicants should provide a description of key elements of the design of that study, including the population to be studied, the setting for delivery of the intervention, primary and secondary outcomes to be assessed, the duration of follow-up, and the statistical analysis to be employed. Investigators may wish to consider assessment of cost-effectiveness as a secondary outcome measure. Applicants should discuss how the proposed pilot and feasibility study, planning project or other effort for which R34 support is requested is related to the full scale trial envisioned under the subsequent R18.

3. **Innovation:** Does the project employ novel concepts, approaches or methods? Are the aims original and innovative? Does the project challenge existing paradigms or develop new methodologies or technologies?

4. **Investigator:** Is the investigator appropriately trained and well suited to carry out this work? Is the work proposed appropriate to the experience level of the principal investigator and other researchers (if any)? Do not include descriptive biographical information.

5. **Environment:** Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support? Do not describe available facilities and equipment.

6. **Translation:** Does the intervention strategy proposed have the ability to be translated into primary care, community, family or other patient care/support settings?

Budget Evaluate direct costs only. The budget is limited to $150,000 per year for two years and should be submitted in the modular format. With regard to personnel, do not be concerned with the salary requested but with the percent effort proposed.

Recommendation If not deferred or recommended for no further consideration, assign a merit descriptor term/priority score.

OTHER CONSIDERATIONS

WOMEN, CHILDREN AND MINORITIES IN STUDY POPULATIONS: Examine whether the minority and gender characteristics of the sample are scientifically acceptable and consistent with the aims of the project, using the categories of 1 to 4 as follows. Determine whether children have been included or appropriately excluded from the study population. (Also determine whether the research is a Phase III clinical trial.)

CODE	Minority (M)	Gender (G)	Children (C)
1	minority and non-minority	both females and males	both children and adults
2	only minority	females only	children only
3	only non-minority	males only	no children included
4	representation unknown	unknown	unknown

Evaluate acceptability as "A" (acceptable) or "U" (unacceptable). If you rate the sample as "U", consider this feature a weakness or a deficiency in the design of the project reflected in the overall scoring of the project. NOTE: To the degree that acceptability or unacceptability impacts on the investigator's approach to the proposed research, such comments should appear under Approach in the five major review criteria above and should be factored into the score as appropriate.

FOREIGN INSTITUTIONS: If the applicant organization is foreign, comment on any special talents, resources, populations, or environmental conditions that are not readily available in the United States or that provide augmentation of existing U.S. resources. In addition, indicate whether similar research is being performed in the U.S. and whether there is a need for such additional research. These aspects do not apply to applications from U.S. organizations for projects containing a significant foreign component.

HUMAN SUBJECTS: If Exemptions are Claimed, express any comments or concerns about the appropriateness of the exemption(s) claimed (e.g., for Exemption 4, is it clear that the information will be recorded by the investigator so that subjects cannot be identified directly or indirectly?). If No Exemptions are Claimed, express any comments or concerns about the appropriateness of the responses to the six required points, especially whether the risks to subjects are reasonable in relation to the anticipated benefits to the subjects and in relation to the importance of the knowledge that may reasonably be expected to result from the research. More detail is provided in the separate set of instructions for evaluating research involving human subjects (also available at http://grants1.nih.gov/grants/peer/hs_review_inst.pdf).

ANIMAL WELFARE: Express any comments or concerns about the appropriateness of the responses to the five required points, especially whether the procedures will be limited to those that are unavoidable in the conduct of scientifically sound research.

BIOHAZARDS: Note any materials or procedures that are potentially hazardous to research personnel and indicate whether the protection proposed will be adequate.

SCIENTIFIC/BUDGETARY OVERLAP: If it is identified in an application, it should be noted in a statement separate from the critique and should not be considered in the evaluation of the application. Identify any overlap of aims or excessive effort between this application and other active or pending support. Reviewers are asked to focus on the scientific and technical merit of the application. The Scientific Review Administrator will ensure that such issues are documented in the summary statement as an administrative note. Purported overlap must be resolved by NIH staff before an award is made.

HUMAN SUBJECTS, ANIMAL WELFARE, AND BIOHAZARDS CONCERNS

Human subjects concerns are important to the NIH. As you evaluate the treatment of human subjects as proposed in the application, please weigh the risks and benefits to the subjects of entering a protocol and indicate whether: (a) they will be at risk as the result of a procedure; (b) an informed consent form has been reviewed by an Institutional Review Board; (c) procedures have been included to deal with potential untoward effects of a treatment; and (d) measures have been taken to protect the anonymity of the subjects. For those applications that deal with human subjects, an indication of concern or no concern should be given as regards treatment of patients. (For more information, see http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm)

In conformance with NIH policy, the use of women, children, and minority individuals in patient populations is an issue that should be addressed in any application which involves clinical research Clinical research includes "...human biomedical and behavioral studies of etiology, epidemiology, prevention (and preventive strategies), diagnosis, or treatment of diseases, disorders or conditions, including but not limited to clinical trials" (OER 90-5). If there is no compelling rationale provided for the exclusion or under-representation of women, children, and minorities from the patient study population, this constitutes a flaw in experimental design and should be reflected in the priority score. Reviewers are asked to inform the Scientific Review Administrator before the review if such concerns exist and to comment specifically on these issues in their critiques. In addition, you will be asked to recommend a code for the application.

NIH policy (http://grants.nih.gov/grants/guide/notice-files/not98-084.html, with additional description at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html) requires that grantees have in place procedures for data and safety monitoring (DSM) activities for all funded clinical trials. This is to ensure the safety of participants, the validity of data, and the appropriate termination of studies for which significant benefits or risks have been uncovered or when it appears that the trial cannot be concluded successfully. The NIH DSM policy covers clinical trials of all phases for which grant support is sought. Applicants must submit a general description of the DSM plan for peer review as part of the grant application. The scientific review group will review this plan and any comments and concerns will be included in an administrative note in the summary statement.

Careful scrutiny also should be given to treatment of animals in experimental protocols. The following issues shall be addressed in the application: (a) identification of the species and approximate number of animals required; (b) the rationale for using animals and the appropriateness of the species and numbers indicated for the work proposed; (c) a complete description of the anticipated use of the animals; (d) an assurance that discomfort and injury to animals will be limited to unavoidable situations and that analgesic, anesthetic, and tranquilizing drugs will be employed where possible to minimize discomfort and pain; and (e) a description of any euthanasia method to be applied. Please indicate in your written critique if you have reason to be concerned over any of these issues.

If biohazardous materials are to be used in the proposed research, the principal investigator should address the proper handling of such items.