

GUIDE FOR ASSIGNED REVIEWERS' PRELIMINARY COMMENTS ON EXPLORATORY/DEVELOPMENTAL GRANT MECHANISM (R21)

The R21 mechanism is designed to support exploratory or developmental research R21 allowing investigators to conduct research on innovative ideas or develop new concepts or technologies. R21 applications generally can only be submitted in response to a specific NIH initiative. Each initiative has its own unique features and often unique review criteria. Maximum duration of award varies by announcement from one to five years, but generally R21s are for two years duration. Budgets can also vary, but are typically between \$75,000 to \$150,000 per year, and thus follow the modular budget requirements. Therefore, before initiating your review of an R21 grant application, the reading of the specific announcement is necessary.

The objective of the R21 grant is to lead to a larger research grant (e.g., R01, P01, U01, etc.) therefore, R21s cannot be renewed. Please use the following guidelines when preparing written comments on R21 grant applications. 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 the goals described in the announcement. NOTE: Your written reviews should not bear personal identifiers because essentially unaltered comments will be sent to the applicant.

The goals of NIH supported research are to advance our understanding of biological systems, to improve the control of disease, and to enhance health. In their written critiques, reviewers will be asked to comment on each of the following criteria in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals. Each of these criteria will be addressed and considered in assigning the overall score, weighting them as appropriate for each application. Note that an application does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, an investigator may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

DESCRIPTION: The NIH now scans the description on page 2 of the application for use in the Description Section of the summary statement. However, as a reviewer you will need to be prepared to provide members of the Study Section sufficient information on the application so that they can follow the critiques and discussion.

CRITIQUE: Include as little descriptive information in this section as possible. Please address each of the following:

Significance: Does this study address an important problem? If the aims of the application are achieved, how will scientific knowledge or clinical practice be advanced? What will be the effect of these studies on the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

Approach: Are the conceptual or clinical framework, design, methods, and analyses adequately developed, well integrated, well reasoned, and appropriate to the aims of the project? Does the applicant acknowledge potential problem areas and consider alternative tactics?

Innovation: Is the project original and innovative? For example: Does the project challenge existing paradigms or clinical practice; address an innovative hypothesis or critical barrier to progress in the field? Does the project develop or employ novel concepts, approaches, methodologies, tools, or technologies for this area?

Investigators: Are the investigators 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? Does the investigative team bring complementary and integrated expertise to the project (if applicable)?

Environment: Does the scientific environment in which the work will be done contribute to the probability of success? Do the proposed studies benefit from unique features of the scientific environment, or subject populations, or employ useful collaborative arrangements? Is there evidence of institutional support?

OVERALL EVALUATION: In one paragraph, briefly summarize the most important points of the Critique, addressing the strengths and weaknesses of the application in terms of the five review criteria. Recommend a score reflecting the overall impact of the project on the field, weighing the review criteria, as you feel appropriate for each application. 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.

PROTECTION OF HUMAN SUBJECTS FROM RESEARCH RISKS: Evaluate the application with reference to the following criteria: risk to subjects, adequacy of protection against risks, potential benefit to the subjects and to others, importance of the knowledge to be gained. If all of the criteria are adequately addressed, and there are no concerns write "Acceptable Risks and/or Adequate Protections." A brief explanation is advisable. If one or more criteria are inadequately addressed, write "Unacceptable Risks and/or Inadequate Protections" and document the actual or potential issue(s) that create(s) the human subjects concern. If the application indicates that the proposed research is exempt from coverage by the human subjects regulations, determine if adequate justification is provided. If the claimed exemption is not justified, indicate "Unacceptable" and explain why you reached this conclusion. Also, if a clinical trial is proposed, evaluate the Data and Safety Monitoring Plan. If the plan is absent, notify the SRA immediately. Indicate if the plan is "Acceptable" or "Unacceptable", and, if unacceptable, explain why it is unacceptable.

NOTE: To the degree that acceptability or unacceptability affects the investigator's approach to the proposed research should appear under "Approach" in the five major review criteria above, and should be factored into the score as appropriate.

GENDER, MINORITY, AND CHILDREN SUBJECTS: Public Law 103-43 requires that women and minorities must be included in all NIH-supported research projects involving human subjects unless a clear and compelling rationale establishes that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. NIH requires that children (individuals under the age of 21) of all ages be involved in all human subjects research supported by the NIH unless there are scientific or ethical reasons for excluding them. Each project involving human subjects must be assigned a code using the categories "1" to "5" discussed below. Category 5 for minority representation in the project means that only foreign subjects are in the study population (i.e., no U.S. subjects). If the study involves both US and foreign subjects use codes 1 through 4. Examine whether the minority and gender characteristics of the subject population comply with NIH policy. For each category, determine if the proposed subject recruitment targets are "A" (acceptable) or "U" (unacceptable). If you rate the sample as "U", consider this feature a weakness in the research design and reflect it in the overall score. Explain the reasons for the recommended codes; this is particularly critical for any item coded "U". Gender (G) Minority (M) Children (C) codes are:

- 1 Both Genders; Minority & nonminority; or Children & adults
- 2 Only Women; Only minority; or Only children
- 3 Only Men; Only non-minority; or No children included
- 4 Gender Unknown; Minority representation unknown; or Representation of children unknown
- 5 Only Foreign Subjects

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. The Five Points on Vertebrate Animals in the Research Plan are:

- Detailed description of proposed use, species/strains, sex, numbers, etc
- Justification of use and numbers
- Veterinary care
- Limitation of discomfort, distress, pain, and injury
- Method of euthanasia.

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

Other comments that may be required, but which do not influence the score are:

BUDGET: Evaluate the direct costs only. Do not focus on detail. Determine whether the total budget is appropriate for the project proposed. Provide a rationale for suggested modification in duration or amount of support.

MODEL ORGANISM SHARING PLAN: All NIH applications that will produce new, genetically modified variants of organisms and related resources are expected to include a sharing plan or to state why sharing is restricted or not possible. Assess the sharing plan in an administrative note. You must take into consideration the organism, the timeline, the applicant's decision to distribute the resource or deposit it in a repository, and other relevant considerations.

FOREIGN: 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.