

Excerpted from PAR-10-197 “NIDDK Multi-Center Clinical Study Implementation Planning Grant Applications (U34)”

The guidelines available here use language posted in the original funding opportunity announcement (FOA) and do not replace or modify the criteria established in the full announcement. If you have any questions, contact the Scientific Review Officer (SRO) in charge of the review panel. SRO contact information for your application can be found in [eRA Commons](#).

NIDDK supports investigator-initiated, multi-center (three or more sites) clinical studies exclusively through a two-part process that includes an implementation planning (U34) grant. The U34 planning grant is designed to: (1) permit early peer review of the rationale for the proposed clinical study; (2) permit assessment of the design and protocol of the proposed study; (3) provide support for the development of documents needed for the conduct of the study, including a manual of operations and (4) support the development of other essential elements required for the conduct of a clinical study.

Completion of the required products of a U34 grant is a prerequisite for submission of a multi-center clinical study cooperative agreement (U01) application, which will support the actual conduct of the study. Pre-approval from NIDDK will be required for submission of an U34 application.

This program announcement, NIDDK MULTI-CENTER CLINICAL STUDY IMPLEMENTATION PLANNING GRANTS (U34), addresses the U34 grant.

Scope

The U34 planning grant process is designed to:

- permit early peer review of the rationale for the proposed clinical study
- permit assessment of the design/protocol of the proposed study
- provide support for finalization of a complete study protocol and development of associated documents and other essential elements of a clinical study.

The activities required in the U34 will depend on the type of study (e.g., epidemiologic study; drug trial, behavior intervention). Activities supported by the U34 include, but are not limited to, the following examples:

- Develop a final study protocol
- Develop consent form(s) and, if applicable, assent form(s)
- Develop an investigator’s brochure or equivalent
- Develop a manual of operations including details, validation, and quality control for any non-standard clinical or laboratory/mechanistic testing which will be performed
- Develop the data monitoring and management plan
- Develop a plan for the acquisition and administration of study agent(s) or device(s)
- Obtain required Office of Human Research Protections assurances if not already in place
- Develop a complete set of suitable documents for submission to the appropriate regulatory authorities
- Develop a safety oversight plan. NIDDK will appoint a DSMB during the U34 phase.
- Develop a detailed budget for conduct and completion of the clinical trial including funding for preparation of a final study report
- Identify clinical study site(s)
- Develop training materials and training/certification plans for study staff
- Initiate the IRB approval process
- Satisfy all regulatory elements of the Food and Drug Administration if an IND is needed for implementation of the research plan
- Negotiate agreements with industry, as needed, to provide drugs, devices, or other resources

In the event of an award, the NIDDK and the Principal Investigator will agree on a list of milestones to be completed during the U34 project period.

Reviewer Guidelines

Written Critiques

- The format of the critiques should follow the structured U34 Critique Template provided on the CD. It can also be downloaded from the Internet Assisted Review (IAR) site in “Meeting Materials”.
- Each core criterion and additional review criteria are represented in the reviewer template and should be commented on, listing the strengths and weaknesses of each.
- In some cases it is perfectly acceptable to use short bulleted sentences as long as your points are clear. However it is also acceptable for you to write a full paragraph or 2 if you feel that is the best way to communicate your impressions. Do not sacrifice clarity in the pursuit of brevity.
- The goal is to provide the maximum and most pertinent information in a concise manner.
- After considering all of the review criteria, briefly summarize the strengths and weaknesses of the application in the Overall Impact section of the template.
- Assigned reviewers must upload critiques before entering an overall impact/priority score.
- Criterion scores should be entered in IAR before the review meeting.
- Assigned reviewers may submit criterion scores only after their critiques have been uploaded. At the SRO's discretion, discussants who are assigned to the application and SRG members who are not assigned to the application may submit criterion scores without critiques.
- The criterion scores may be changed during FINAL SCORING on your electronic or paper Voter/Scoring Sheet, or following the review meeting during the EDIT phase.
- Please do not write your criterion scores on the critique template.

Preliminary Scores

- Each of the five (5) core review criterion (Significance, Investigators, Innovation, Approach, and Environment) should be given a score using the nine-point rating scale (1 to 9, Best to Worse) in accordance with the new Enhanced Peer Review Criteria.
- The criterion scores for the applications should be entered in the meeting Internet Assisted Review (IAR) site in NIH Commons before the review meeting using the same page that is used for submitting the preliminary impact/priority score and critique.
- The criterion scores may be changed following the review meeting during the EDIT phase.
- In the READ phase of the meeting reviewers may submit their scores and critiques, but may not edit them. Core criterion scores can be submitted only after your critique had been uploaded into IAR.
- The criterion scores will appear in the summary statement as part of your critique.

Review Criteria

Overall Impact: Reviewers will provide an overall impact/priority score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following five scored review criteria, and additional review criteria (as applicable for the project proposed).

Scored Review Criteria

Reviewers will consider each of the five review criteria below in the determination of scientific and technical merit, and give a separate score for each. An application does not need to be strong in all categories to be judged likely to have major scientific impact. For example, a project that by its nature is not innovative may be essential to advance a field.

Significance: Does the project address an important problem or a critical barrier to progress in the field? If the aims of the project are achieved, how will scientific knowledge, technical capability, and/or clinical practice be improved? How will successful completion of the aims change the concepts, methods, technologies, treatments, services, or preventative interventions that drive this field?

- Does the background support the rationale for the study?
- Are the study objective(s) and hypothesis(es) adequately defined?
- Is the significance and need to perform a future clinical study adequately justified?
- Would the results of the proposed study be likely to affect health care policy or practice in the specific area of research?
- If mechanistic studies are proposed, are they appropriate and will they provide important scientific information?

Investigator(s): Are the PD/PIs, collaborators, and other researchers well suited to the project? If Early Stage Investigators or New Investigators, or in the early stages of independent careers, do they have appropriate experience and training? If established, have they demonstrated an ongoing record of accomplishments that have advanced their field(s)? If the project is collaborative or multi-PD/PI, do the investigators have complementary and integrated expertise; are their leadership approach, governance and organizational structure appropriate for the project?

- Is the expertise and ability of the investigator and the clinical study team sufficient to organize and manage complex projects?
- Is the investigator and the clinical study team appropriately trained with suitable potential to develop and execute the proposed study?
- Is the work proposed appropriate to the experience level of the investigator and the research team?
- Are appropriate resources and/or other key personnel identified?
- Is there clear evidence of scientific and administrative leadership?

Innovation: Does the application challenge and seek to shift current research or clinical practice paradigms by utilizing novel theoretical concepts, approaches or methodologies, instrumentation, or interventions? Are the concepts, approaches or methodologies, instrumentation, or interventions novel to one field of research or novel in a broad sense? Is a refinement, improvement, or new application of theoretical concepts, approaches or methodologies, instrumentation, or interventions proposed?

Approach: Are the overall strategy, methodology, and analyses well-reasoned and appropriate to accomplish the specific aims of the project? Are potential problems, alternative strategies, and benchmarks for success presented? If the project is in the early stages of development, will the strategy establish feasibility and will particularly risky aspects be managed?

- If the project involves clinical research, are the plans for 1) protection of human subjects from research risks, and 2) inclusion of minorities and members of both sexes/genders, as well as the inclusion of children, justified in terms of the scientific goals and research strategy proposed?
- Will the study concepts and design, methods, and analyses, including preliminary statistical analyses, successfully accomplish the aim(s) of the proposed clinical study?
- Are the activities proposed for the planning period adequate (Refer to the Scope section above)?
- Will the activities proposed be sufficient to allow for timely and successful study implementation?
- Will the proposed planning activities address all major barriers to the future clinical study?
- Are the administrative plans for the management of the research project appropriate, including plans for resolving conflicts?

Environment: Will the scientific environment in which the work will be done contribute to the probability of success? Are the institutional support, equipment and other physical resources available to the investigators adequate for the project proposed?

- Will the project benefit from unique features of the scientific environment, subject populations, or collaborative arrangements?
- Are there adequate plans for the development of an effective organizational structure for carrying out the proposed study?
- Is the study population required for the proposed study available?

Additional Review Criteria

As applicable for the project proposed, reviewers will consider **the following additional items in the determination of scientific and technical merit, but will not give separate scores for these items.**

Protection of Human Subjects from Research Risk: The For research that involves human subjects but does not involve one of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate the justification for involvement of human subjects and the proposed protections from research risk relating to their participation according to the following five

review criteria: 1) risk to subjects, 2) adequacy of protection against risks, 3) potential benefits to the subjects and others, 4) importance of the knowledge to be gained, and 5) data and safety monitoring for clinical trials.

For research that involves human subjects and meets the criteria for one or more of the six categories of research that are exempt under 45 CFR Part 46, the committee will evaluate: 1) the justification for the exemption, 2) human subjects involvement and characteristics, and 3) sources of materials.

Inclusion of Women, Minorities and Children in Research: When the proposed project involves clinical research, the committee will evaluate the proposed plans for inclusion of minorities and members of both genders, as well as the inclusion of children.

Vertebrate Animals: The committee will evaluate the involvement of live vertebrate animals as part of the scientific assessment according to the following five points: 1) proposed use of the animals, and species, strains, ages, sex, and numbers to be used; 2) justifications for the use of animals and for the appropriateness of the species and numbers proposed; 3) adequacy of veterinary care; 4) procedures for limiting discomfort, distress, pain and injury to that which is unavoidable in the conduct of scientifically sound research including the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices; and 5) methods of euthanasia and reason for selection if not consistent with the AVMA Guidelines on Euthanasia. For additional information, see <http://grants.nih.gov/grants/olaw/VASchecklist.pdf>.

Biohazards: Reviewers will assess whether materials or procedures proposed are potentially hazardous to research personnel and/or the environment, and if needed, determine whether adequate protection is proposed.

Resubmission Applications: When reviewing a Resubmission application (formerly called an amended application), the committee will evaluate the application as now presented, taking into consideration the responses to comments from the previous scientific review group and changes made to the project.

Revision Applications: When reviewing a Revision application (formerly called a competing supplement application), the committee will consider the appropriateness of the proposed expansion of the scope of the project. If the Revision application relates to a specific line of investigation presented in the original application that was not recommended for approval by the committee, then the committee will consider whether the responses to comments from the previous scientific review group are adequate and whether substantial changes are clearly evident.

Additional Review Considerations

As applicable for the project proposed, reviewers will address each of the following items, but will not give scores for these items and should not consider them in providing an overall impact/priority score

Applications from Foreign Organizations: As applicable for the FOA or submitted application, reviewers will assess whether the project presents special opportunities for furthering research programs through the use of unusual talent, resources, populations, or environmental conditions that exist in other countries and either are not readily available in the United States or augment existing U.S. resources.

Select Agents Research: Reviewers will assess the information provided in this section of the application, including 1) the Select Agent(s) to be used in the proposed research, 2) the registration status of all entities where Select Agent(s) will be used, 3) the procedures that will be used to monitor possession use and transfer of Select Agent(s), and 4) plans for appropriate biosafety, biocontainment, and security of the Select Agent(s).

Resource Sharing Plans: Reviewers will comment on whether the following Resource Sharing Plans, or the rationale for not sharing the following types of resources, are reasonable: 1) Data Sharing Plan (Not Applicable); 2) Sharing Model Organisms (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-04-042.html>); and 3) Genome Wide Association Studies (GWAS) (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-07-088.html>).

Budget and Period of Support: Reviewers will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research budget and the appropriateness of the requested period of support in relation to the proposed research may be assessed by the reviewers. The priority score should not be affected by the evaluation of the budget.