

1. May the extramural partner be a U.S. owned domestic for profit organization, small business or otherwise?

The eligibility criteria include for-profit organizations, which would include small businesses, but foreign applicants and foreign components are not eligible.

2. Are there any special small business clauses that will be applied in the case of this U01?

This is not a Small Business Innovation Research (SBIR) solicitation. The standard conditions of a U01 application apply to all applicants. Detailed information may be found in the NIH Grants Policy Statement:

(http://grants.nih.gov/grants/policy/nihgps_2010/index.htm)

3. Is it required that a non-profit or extramural academic institution must be involved in the project?

No. Projects must include both an intramural investigator and a non-NIH investigator, and the application may be submitted by any of a number of eligible institutions. For more details, see the list of eligible institutions as described in the Funding Opportunity Announcement (FOA): <http://grants.nih.gov/grants/guide/pa-files/PAR-13-029.html>

4. Are there any restrictions on federal agency participation, like DARPA or HHS?

As described in the Funding Opportunity Announcement (FOA) “eligible agencies of the federal government” may apply.

5. Are there any product development or translational objectives associated with this solicitation?

Evaluation of therapeutic devices is encouraged but not required. Each application will be evaluated on its scientific merit.

6. Is it necessary to have an FDA approved IND at the time of application?

No.

7. Could you expand on the details regarding the leadership plan (related to multiple PIs)?

Multiple PI projects are required to include a section describing the leadership plan. This plan should describe the governance and organizational structure of the research

project, including communication plans, process for making decisions on scientific direction, allocation of resources, publications, intellectual property issues, and procedures for resolving conflicts. Examples of leadership plans are available on the Multiple PI website at: http://grants.nih.gov/grants/multi_pi/index.htm

For this FOA, the (non-NIH) extramural investigator should be designated as the “contact PI” if the Multiple PI option is used.

8. Can a project have two extramural PIs and a PI from Intramural? In other words, have three PIs.

Certainly. The application comes from the applicant institution, and that organization submits the application on behalf of the PI(s). The extramural PIs would have to meet the requirements of the respective institution(s).

There is no limit to the number of PIs, but the more PIs the more complex your plan becomes. There can be more than one intramural PI as well.

9. The study I would like to propose in response to this opportunity will only require sending samples taken from patients to NIH for further analysis. Patients will not be going to the NIH Clinical Center for further management. Will this type of study qualify for this opportunity?

One of the requirements is that some work be done at the Clinical Center. The project you described is not excluded from consideration, provided there is collaboration. Along with some work at the Clinical Center, key components will be collaborations and novel work to meet this FOA’s intent.

10. What is the percentile pay line for this program?

These are not R01 awards, so they would not necessarily be restricted by the R01 pay line considerations. Each institute will make decisions about awards on the basis of their research priorities, programmatic needs, and availability of funds at the time.

11. A concern is that the budget may not be adequate to cover the costs of a clinical trial especially if, for example, manufacture of a GMP grade specialized blood is required for this study and cannot be accomplished using NIH Intramural resources.

We’re anticipating resources required in the grant will indeed be possible through the NIH Clinical Center’s departments. The costs for each project are going to be determined up-front, depending on the specific research plan. The cap is \$500,000, and the grant has to be funded within that limit. Rates for Clinical Center resources have been developed with the intent of only recovering the marginal costs of CC services. If a cohort or patient is already being seen at the Clinical Center there will be no new costs for the care of those patients except if a new approach is being taken. For example, if

you want to do PET scanning on one hundred patients who were not receiving PET scans for other reasons, then, there would be an added cost. But the grant will not have to pay the daily costs for the patient being seen for routine inpatient or outpatient visits already ongoing before the start of the grant. In addition, the budget would not need to include any salary support for intramural investigators. Therefore, the Clinical Center believes much project work can be done within the resources defined. Please contact the Clinical Center early to help build and understand your budget.

12. What if multiple NIH Institutes are involved, as could happen if vector production is coming from NHLBI, clinical treatment provided by NCI, and HIV assays by NIAID. Do we need multiple intramural investigators and will the main PI interact with other NIH resources to facilitate the collaboration?

Like any NIH grant, there needs to be a primary institute. Designation of the primary institute is something that would have to be discussed among the investigators and the staff at those institutes. Once a primary institute is identified, there may be one or more secondary institutes. In this example, secondary institute assignment would seem appropriate. The number of intramural investigators involved would also need to be discussed among the participating institutes, and would depend upon the scientific and technical expertise needed to conduct the project. The program contacts listed in the FOA can facilitate the kinds of discussions between institutes that would need to take place for such a research project.

13. When you say no foreign components, can we not even be a part of a research project if we are not requesting funding for the foreign site? If a Canadian site is mentioned, will this be automatic denial of the application?

For this announcement, we are not considering foreign components.

14. Is it possible to have a foreign consultant if no foreign components are involved?

There is a difference between consultant and component. Foreign consultants can be accommodated.

15. What exactly is meant by a “foreign component”?

A “foreign component” is defined in the NIH Grants Policy Statement (http://grants.nih.gov/grants/policy/nihgps_2012/nihgps_ch1.htm http://grants.nih.gov/grants/policy/nihgps_2012/nihgps_ch16.htm#foreign_grants)

Foreign Component: The performance of any significant scientific element or segment of a project outside of the United States, either by the grantee or by a researcher employed by a foreign organization, whether or not grant funds are expended. Activities that would meet this definition include, but are not limited to, (1) the involvement of human subjects or animals, (2) extensive foreign travel by grantee

project staff for the purpose of data collection, surveying, sampling, and similar activities, or (3) any activity of the grantee that may have an impact on U.S. foreign policy through involvement in the affairs or environment of a foreign country.

Examples of other grant-related activities that may be significant are:

- collaborations with investigators at a foreign site anticipated to result in co-authorship;
- use of facilities or instrumentation at a foreign site; or
- receipt of financial support or resources from a foreign entity.

Foreign travel for consultation is not considered a foreign component.

16. Can you elaborate further about a project that might lead to international collaboration?

Although this grant will not fund foreign institutions, if an application proposes to develop a vaccine that might ultimately be tested at an international site, then that kind of project may be very well received depending on the work proposed and institute programmatic alignment. This grant, however, could not support the international work.

The specific details of such a project should be discussed with the appropriate staff contacts.

17. Is there any advantage to involving multiple institutes in an application?

It depends. The practical advantage is mainly scientific and intellectual collaboration. Disadvantages could be the costs and complexity. The investigators will have to determine what will be the best way to conduct the project and achieve the scientific goals.

18. Are Clinical Center investigators eligible to be the sole collaborating intramural investigator?

The Clinical Center investigators are not in an organization which has funding authority. A Clinical Center investigator may be the sole collaborating intramural investigator, provided there's a sponsoring NIH institute that's willing to fund the grant.

19. Do all applications have a clinical trial component or can you have a translational research study that does not have a clinical trial?

Yes, translational research studies are eligible.

20. At the time of the submission deadline, March 20th, does a clinical protocol need to be IRB approved? If not, at what level of development should the clinical protocol be at the time of submission of the application?

IRB approval is one of the “just-in-time” requirements. IRB approval is not needed to submit an application, but would be needed in order to receive an award. Depending on where the clinical study was done -- at the extramural institution and/or at the Clinical Center -- there may potentially need to be more than one IRB review.

21. Will there be a multi-project announcement following the current operation with opportunities for collaborative opportunities at the Clinical Center?

A multi-project announcement may occur in the future, however this pilot initiative must first be evaluated.

22. Could you please review the indirect cost allocation issues between intramural and extramural?

The extramural institution is provided indirect costs in accordance with their indirect cost (F&A) rate at time of award. For the NIH portion of the project, there's no allocation of indirect costs.

23. Is it expected or necessary that the extramural and intramural PIs have previously collaborated on publications?

No. Applicants to this program may propose new collaborative partnerships.

24. Will one of the criteria for funding be that the proposed project result in a population of patients being seen at the Clinical Center that currently are not being seen there?

No, this is not a requirement.

25. Is this program applicable to collaborations involving clinical data previously obtained from the Clinical Center? For example, facilitating analysis to existing data or augmentations of clinical database analysis and integration capabilities.

It would depend upon the merit of the proposed project.

26. Can funds to the intramural investigator pay for the hiring of a contract research nurse or nurse practitioner to help carry out the clinical study if existing personnel are not sufficient?

Yes, this is allowable.

27. Will the funds come from the existing intramural budget of the IC or will new funds be available so the U01 will not compete for existing funds?

Each institute will determine how to fund these awards, and there will be flexibility within that institute on how to structure the intramural funding.

28. Can you give us an estimate of what the costs are to take a new vaccine product sub unit antigen through toxicity and GMP? Do you think it's possible to go through it with the dollars available? Who is the contact person to get a budget estimate?

We would have to know more specifics of the planned vaccine product. We suggest you start by contacting Pat Piringer in the Clinical Center (ClinicalCtrPartner@mail.nih.gov; 301-496-4121) or the scientific contact for the institute most relevant to your research. These individuals are listed in the FOA.

29. In terms of collaboration, can it be related to development, deployment, and assessment of a tool to enable a clinical assessment in the Clinical Center or must the nature of the collaboration be focused on hypothesis-driven scientific research?

It can be a hypothesis-generating proposal. For example, one could look at data in the vast resources within the Clinical Center or some other institution. A proposal might not include a hypothesis initially. A hypothesis might be generated as information is collected. There may be an observational study that can lead to a general hypothesis, like one of the natural history protocols for rare diseases that we currently have at the Clinical Center. It wouldn't be an absolute requirement at the beginning, but we do expect that the project will lead to a hypothesis-type trial protocol.

30. Are sub-contract sites allowed separate from the multiple PI plan?

As long as the project has the required collaboration -- one intramural investigator and one extramural investigator -- then yes, a sub-contract would be allowed.

31. What sign-off documents are needed from the NIH personnel at the Clinical Center?

The application will need to include a Letter of Support/Collaboration from the Director of the Clinical Center.

32. Are Intramural Investigators at the National Institute of Drug Abuse (NIDA) Baltimore campus eligible to collaborate on this project?

If their Scientific Director approves their collaboration and the sponsoring institute approves their collaboration (as evidenced by a Letter of Support / Collaboration), then yes, they may participate. Keep in mind, however, that some project work must be done at the NIH Clinical Center.

33. How is the budget structured? According to the RFA we need to ask for direct costs for research activity in both collaborating centers.

The budget requirements are well described in the FOA, and yes, the budget should account for the costs of the extramural investigator(s), the intramural investigator(s), and the Clinical Center. If there are further questions investigators should contact Pat Piringer in the Clinical Center (ClinicalCtrPartner@mail.nih.gov; 301-496-4121).

34. How many awards do you anticipate making in this round of funding?

This is not an RFA, which has set-aside funds. The number of awards made will depend upon the scientific merit of the applications, how well the applications match with programmatic interest, and the availability of funds at the relevant NIH institute.

35. Could you clarify whether out-and-out method development would be legitimate?

Absolutely. For example, if an applicant proposes to develop a diagnostic tool, that would be appropriate.

36. Would an application from a Clinical Center Principal Investigator be at a disadvantage for consideration if the application lacked a Co-Principal Investigator from the funding institute?

Not necessarily. If the Clinical Center Investigator can get support from one of the participating institutes (signified by a Letter of Support from that institute), that would be sufficient.

37. In a multiple PI application, one extramural and two intramural PIs, can one of the two intramural PIs be from one of the institutes that does not currently support the U01 program?

Yes, certainly. The sponsoring institute must indicate willingness to support all intramural costs via a Letter of Support.

38. Is translational research allowed with the treatment plan at both the intramural and the extramural institutes?

Yes.

39. My intramural collaborator's institute is not participating in the FOA. How might I participate in this initiative?

If one of the participating institutes is willing to support the project's intramural costs, there is no issue. But, you must have a sponsoring institute, as indicated by the Letter of Support.

40. Does the \$500,000 direct cost annual cap include intramural and extramural funds?

Yes.

41. What should be included in the Letter of Intent?

As described in the FOA and shown on the presentation slides, the Letter of Intent should include:

- Descriptive title of proposed research
- Name(s), address(es), and telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating institution(s)
- Number and title of this funding opportunity (PAR-13-029)

The LOI may also include:

- Brief research plan
- Summary of the Clinical Center services planned for utilization

The Letter of Intent can serve as your request for the Letters of collaboration/support from the Clinical Center and the relevant IC which are required for a complete application.

42. How is the IRB review process handled and what active protocols will be involved in multiple sites?

The IRB review process will vary for each project.

The investigators may consult with Charlotte Holden (Charlotte.Holden@nih.gov) or Peg Sanders (sandersmh@nih.gov) in the NIH Office of Human Subjects Research regarding this question. IRB review may occur at each site, or alternatively, it may be possible to enter into an Authorization Agreement (also known as a "reliance agreement"). This is an agreement between NIH and one or more institutions involved in the same cooperative research that assigns regulatory responsibilities to specific IRBs. You can read more about reliance agreements at

<http://www.niaid.nih.gov/LabsAndResources/resources/toolkit/Pages/faq.aspx>

A multi-site protocol may have two Principal Investigators, with one for each institution.

IRB approval is not required before grant submission, but it is required before the grant is awarded.

43. Just a clarification on the IRB approval question. If a clinical protocol is included as part of the application but its initiation is dependent upon a successful IND following for a new GMP material to be produced at the Clinical Center as part of the collaboration, can the IRB approval be deferred beyond the initial JIT period or award? For example, a protocol submitted for IRB review late in funding year one or two for a trial late in years two and three?

Yes. Each project is going to be looked at individually. For example, an investigator may propose a very compelling project to design a new drug that requires IND approval, but the protocol can't obtain IRB approval because you don't have the product yet. Funding would, of course, depend on the scientific merit of the project.

It's possible to have a grant application where there are several steps in the research plan and perhaps the last step is not fully defined or has uncertainties. We sometimes refer to this as "delayed onset" human subject research. In such cases, the first part of the project can be done with the existing approval, but then additional approvals might be needed before those other parts of the project can proceed.

44. Who is the best person to contact with respect to a project idea for this FOA? The contact person listed in the FOA, at the institute most likely to be interested in the idea. I guess that would be extended to the intramural collaborators as well.

The scientific/research contacts at the relevant institute are listed in the FOA. These individuals would be your first point of contact. They can discuss the institute's research interests and help shepherd your request, identifying other contacts as needed.