Technical Assistance Webinar for RFA-AT-20-003, Emotional Well-Being: High-Priority Research Networks (U24, Clinical Trial Optional)

March 17, 2020

Purpose of the Webinar

On Tuesday, March 17, 2020, the National Institutes of Health (NIH) National Center for Complementary and Integrative Health (NCCIH), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), and National Institute on Aging (NIA) hosted a preapplication webinar to provide information about the funding opportunity announcement (FOA) for Emotional Well-Being: High-Priority Research Networks (U24, Clinical Trial Optional), RFA-AT-20-003.

Webinar Speakers

- Merav Sabri, Ph.D., Program Director, Division of Extramural Research, NCCIH
- Rosalind King, Ph.D., Associate Director for Prevention and Health Scientist Administrator, Population Dynamics Branch, Division of Extramural Research, NICHD
- Lis Nielsen, Ph.D., Director, Division of Behavioral and Social Research, NIA
- Jessica M. McKlveen, Ph.D., Health Scientist Administrator (Scientific Review Officer), NCCIH
- Anita McRae-Williams, M.A., Outreach Communications Program Manager, Division of Extramural Research, NCCIH (Webinar Moderator)

Background

Dr. Sabri explained that emotional well-being is a high-priority research topic for NCCIH. It was the focus of a 2018 roundtable discussion, which was a precursor to this funding opportunity. The objectives of the funding opportunity are:

1. Develop transdisciplinary networks designed to advance research on emotional well-being
2. Propose new, high-impact activities to advance at least one (minimum) and up to three (maximum) high-priority areas
3. Propose to support activities and/or produce resources that will serve the field.

An application that is a discretely bounded research project is not appropriate for the U24 funding mechanism.

Areas of Interest

The specific areas of interest of this RFA are ontology and measurement, mechanisms, biomarkers, the relationship between emotional well-being and prevention, technology and outcome measures for mechanistic studies, and development and validation of emotional well-being measures.

The Structure of a U24 Mechanism

NIH, in collaboration with the awarded networks' Program Director(s)/Principal Investigator(s) (PD(s)/PI(s)), will establish post award an emotional well-being Consortium Steering Committee. The

Steering Committee will be composed of NIH Project Scientist(s) and additional designees of NIH, and each network's PI(s)/PD(s) and coinvestigators as deemed necessary.

The goal of a U24 grant mechanism is to facilitate research networks through innovative activities including small-scale pilot research. Other activities include systematic reviews, data resources, workshops, and workshop reports to foster the growth and development of research in the priority areas.

The three participating institutes and centers (ICs) expect to support a total of two or three awards.

- Dr. Sabri explained that NCCIH's areas of interest include both mind and body practices and natural products used in the context of whole person health. NCCIH's mission is not specific to one disease or organ system. NCCIH seeks to understand how complementary health approaches affect health, resiliency, and well-being across the lifespan in diverse populations.

- Dr. King explained that NICHD's specific interest for this FOA is in advancing the measurement of quality of life as an indicator of emotional well-being in two populations: (1) pediatric populations (across all of childhood and adolescence), and (2) populations with intellectual and developmental disabilities. NICHD is interested in networks that will validate measures in these populations, define the lower limits of age or cognitive functioning for reliability in self-report, or develop novel measures and enhance understanding of the relationship between subjective and objective measures of emotional well-being.

- Dr. Nielsen said that NIA has been studying subjective well-being for nearly two decades, including measurement development, population-based data collection, and international collaborations. The scope of the science of interest to NIA is (1) promoting a life-course approach to explanations for both positive and negative health outcomes, (2) exploring midlife opportunities for interventions to reverse or redirect adverse aging processes and promote successful or adaptive aging, and (3) studying the positive aspects of lifespan development, including purpose and well-being. NIA is interested in understanding the determinants of positive health, as well as well-being metrics that signal when individuals and societies are doing well. Measurement of subjective or emotional well-being in aging is important for its causal role in promoting behavior change or as an intervention target and as an end in itself, to maximize positive aspects of well-being.

Previous Networks

Dr. Nielsen presented two examples of networks previously funded by NIA under the R24 mechanism, one on stress measurement in large population-based datasets and one on biomarkers. These networks are similar to the ones that will be funded under the current RFA. Links to both networks are included in the slide set.

Here are examples of networks submitted in response to similar RFAs:

- The Biomarker Network: http://gero.usc.edu/cbph/network/
- Stress Measurement Network: https://stresscenter.ucsf.edu/
- Decision Neuroscience Network: https://www.decisionneuroaging.network/

Factors That Impact Review

Dr. McKlveen explained that applications that are incomplete, noncompliant, or nonresponsive to the RFA may not be accepted for review.

- To be **responsive**, applications must propose network activities in at least one and up to three of the six priority areas identified in the Funding Opportunity Scope section of the RFA. Specific foci within a priority area must be defined. Applications proposing other areas of inquiry will be deemed nonresponsive.
- The **scope** of network activities must include dissemination activities, pilot projects, and collaboration, like an annual meeting of all the networks funded under this announcement to share advances. Applications must articulate clear milestones and criteria for evaluating success of their dissemination, pilot research, and collaboration efforts.

Compliance requirements include:

- Budget: May not exceed $400,000 per year in direct costs
- Project Period: Up to 4 years
- Eligibility: Foreign components are allowed, but foreign institutions and non-U.S. components of U.S. organizations are not
- Page Limitations: 1 page for Specific Aims; 12 pages for Research Strategy
- The due date for allowable post-submission materials is 30 calendar days before the peer review meeting date. Applicants should consult NOT-OD-19-083 for allowable post-submission materials. Information accidentally left out of the application cannot be submitted as post-submission material.

Completeness requirements include

- Submission of a Study Record for any study that meets the definition of a clinical trial
- Inclusion of a Resource Sharing Plan.

Applications will be scored according to the five standard review criteria (significance, investigator(s), innovation, approach, and environment), plus additional review criteria. Language specific to this RFA has been added to each of the five standard criteria (and is highlighted in red text on the slides for this webinar). The additional criteria include the study timeline (for clinical trials only), milestones, and the Resources and Data Sharing Plan, as well as the usual criteria of protections for human subjects, inclusion plans, vertebrate animals, and biohazards.

Applications will be reviewed in a **Special Emphasis Panel** at NCCIH. Reviewers will be selected based on their specific area of expertise in the target areas of the RFA and the science proposed in the applications, and they will be oriented about the additional review language and additional review criteria added to this FOA and to be used in their assessment. Applicants should keep in mind to address how their application would be impactful considering the goals of the RFA.

Letters of intent (optional but appreciated) are due to Dr. Martina Schmidt at NCCIH on March 22, 2020. The application due date is **April 22, 2020**. The review meeting will be held in July 2020, and the roster will be available 30 days before the meeting. The award decisions will be made in October 2020.

Questions and Answers

Emmeline Edwards, Ph.D., director of NCCIH's Division of Extramural Research, joined the webinar to help answer participants' questions. Ms. McRae-Williams explained that Dr. Edwards has been a driving force behind placing emotional well-being as a high priority at NIH.

Q: Which institute will fund my proposal? And does the application need to appeal to all three institutes?

A: Dr. Sabri explained that once all the applications are received, the ICs will determine their interests based on the science and make funding decisions based on the review criteria and the relevance of proposed projects to their program priorities. Dr. Edwards added that there might be situations in which ICs would cofund an award.

Q: Is there a requirement regarding the proportion of direct costs that should be allotted for pilot research both annually and totally?

A: Dr. Edwards explained that investigative teams are being given the discretion to prepare their budgets and justify them appropriately. The goal of the pilot work is that at the end of the 4-year period, the team should be fully prepared to submit an application under the R01 mechanism or another research funding mechanism at NIH.

Q: If the network comprises many institutions, how do we fund pilot projects at institutions other than the one to which the grant is awarded?

A: Dr. Nielsen explained that in prior R24s similar in structure to this network, many institutions awarded pilot projects as stipends to investigators. Sometimes a flat sum was used. Arrangements can be worked out between the participating institutions.

Q: Are there any disallowed expenses for overall budgets or pilot studies?

A: Dr. McKlveen explained that the institution's grants management office makes these policy decisions, so the PI would need to work with their institution's grant management office to discuss the budget and determine what's allowable.

Q: Please describe the recommended strategies for being responsive to the requirement for multiple research sites.

A: Dr. Nielsen explained that ideally, the intellectual leadership of the network would be housed at a couple of institutions, and networks would also include others outside their own institution in their activities. Support at the home institution(s) is also important. This doesn't have to be a massive multi-institution award, but typically, you would not find expertise on all the topic areas at one institution.

Q (submitted by potential first-time applicant): In the optional letter of intent, are just the names of key personnel required, or should we also submit information about positions and departments? Is no description of the project needed beyond the title?

A: Dr. McKlveen explained that information on this topic is in section 4 of the RFA. Required information includes the name(s), address(es), and telephone number(s) of the PI(s); the names of other key personnel; and the name(s) of the institution(s). No information about personnel beyond that is

required. The only information needed about the proposed project is a descriptive title of the proposed activity; however, applicants are welcome to include more information.

Q: Is it a good idea to include multiple PIs, or should one person be designated as PI, with other collaborators in non-PI status?

A: Dr. Nielsen said that both approaches are possible, and both types of applications have come in for networks in the past.

Q: Would you recommend a less experienced early stage investigator as PI or a more experienced one who might have less time to devote to the project?

A: Dr. King explained that there is no new or early stage investigator preference associated with this funding mechanism. The PI(s) should be the true intellectual leader(s) who will be doing the work and "leading the charge" and who are well suited to do those things.

Q: Do you know who will be on the special review panel? How can we find out?

A: Dr. McKlveen explained that reviewers will be recruited specifically for the Special Emphasis Panel. The roster will be published 30 days prior to the review meeting. There will be a "View Meeting Roster" link in the eRA Commons folder for submitted applications.

Q: What should the outcomes of the annual meeting be, and can the meetings be remote?

A: Dr. Sabri explained that the annual meeting is an in-person meeting. PIs and coinvestigators, as well as other key personnel deemed necessary, are expected to attend, and the budget must include the cost of their travel. Any other travel related to the pilot studies also needs to be part of the calculation. Dr. Nielsen added that the purpose of the meeting is to exchange ideas across the network to make sure all groups are on the same page, to avoid duplication of effort, and to allow for cross-pollination of ideas, so finding good ways to exchange information is important. Dr. Edwards explained that the in-person meeting will help build the research community in this field. The field is fairly young, and NIH wants to bring people together who will work together.

Q: Does NIH have a population they're most interested in?

A: Dr. Nielsen explained that there isn't one specific population that is the focus. The three ICs have a very broad focus and are interested in life course research. The purpose of this initiative is to support activities that strengthen and advance well-being research for the field at large. If a proposal also serves the needs of specific populations, that's a plus. Dr. King noted that NICHD may have some target populations in mind, but that doesn't speak for the entire initiative. Applicants should think about what they're best suited to study.

Q: Does prevention research encompass strategies, treatments, or interventions aimed at promoting emotional well-being?

A: Dr. Nielsen said that the answer is yes. The goal of an intervention could be emotional well-being as an end in itself, or intervention research could look at modifying aspects of emotional well-being to foster a further outcome. Emotional well-being could be a predictor, mediator, or target.

Q: Can you speak a little more on the balance between demonstrating that you have a network at the time of application but not too large of a network that then introduces conflict?

A: Dr. Nielsen explained that if your application includes every person you envision as part of your research network, it creates conflicts of interest with review. It's better to articulate your own expertise to lead activities and identify additional types of expertise that you hope to engage as you go forward. Your team should have sufficient expertise to lead the activities, and you should make clear what other expertise you will seek. Dr. McKlveen emphasized the need to avoid creating additional conflicts of interest.

Q: For the proposed pilot projects, do you want to see a specific research plan or just the process for making these available to the network?

A: Dr. Sabri explained that there could be different scenarios. The proposal could include detailed ideas for a pilot or two but at the same time provide plans for outreach, describing the other types of pilot projects you would be soliciting and the expertise you're looking for from the field in general. If you are not ready to plan your pilot projects, you could include a plan for how you would solicit and evaluate potential pilot projects. What are the criteria you would use to evaluate them?

Q: Do we have any guidelines for the scope of a pilot project?

A: Dr. Nielsen explained that pilot projects are designed to address specific questions identified by the network. They could be wide-ranging open questions, or they could be very small-scale work, such as a literature review or harmonizing datasets. The nature of the pilot projects depends on the goals of the network and how they are best accomplished.

Q: Would a proposal involving a population of pregnant women be responsive to this RFA?

A: Dr. King explained that the RFA deals with the whole life course, and pregnancy is part of that, so it is part of the ICs' collective interests.

Q: Would an application focused on the well-being of health care providers be responsive, especially if linked to patient outcomes?

A: The goal is to develop resources for the field at large (e.g., resources that will strengthen the conduct of well-being interventions broadly), not just to support specific projects.

Q: If a proposal encompasses three different areas but is focused only on health professional well-being, would it fit this RFA?

A: Dr. King said that if that population is useful for illuminating questions that will advance the entire field, it could be considered.

Q: What do panelists think about the conceptual overlap or distinction between subjective and emotional well-being?

A: Dr. Nielsen said that part of the goal of the RFA is developing an ontology and working on measurement development, including tackling this issue and adding clarity to the research field.

Q: Could you clarify how to engage foreign components in the absence of involving foreign institutions? Can collaborators be paid through a non-U.S. institution, such as a university?

A: Dr. McKlveen explained that foreign components are allowed. They could serve as consultants or be named as key personnel or coinvestigators. However, foreign institutions or foreign components of U.S.-based institutions are not allowed. A foreign component is defined as "the performance of any significant scientific element or segment of a project outside of the United States, either by the recipient 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 recipient project staff for the purpose of data collection, surveying, sampling, and similar activities, or (3) any activity of the recipient 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."

Q: Would you expect the meetings to be open only to those involved directly with the grant or a larger type of conference or symposia?

A: Dr. Edwards and Dr. Sabri explained that the in-person annual meeting will not be open to the public.

Q: Can funds be budgeted to attend other conferences relevant to the area but not organized by grant personnel?

A: Dr. Nielsen said yes, but you would have to justify the use of the resources.

Q: What's the difference between a U24 and an R24 in terms of funding, structure, or intent?

A: The U24 is a cooperative agreement, which means there is substantial involvement of NIH staff to help ensure the initiative meets its milestones and to facilitate collaboration. The R24 is completely coordinated and organized by the PIs.

Q: Dr. Sabri said that all key personnel must budget for travel to the in-person meeting. Does this apply only to PIs or to all key personnel?

A: Dr. Sabri explained that in some cases it might be important for key personnel not designated as PIs or co-PIs to attend the meeting. An estimate of the number of those individuals should be included in the budget. These meetings will provide opportunities to share advances across networks, promote collaboration, and avoid duplication of efforts.

Q: Considering the populations you're focusing on, would families and their emotional well-being be relevant to this U24?

A: Dr. King explained that the family as a context for emotional well-being is of interest to all three ICs.

Q: Do you have any concerns about subcontracts in the overall budget for different components of the grant or eventual funding of pilot projects?

A: Dr. Sabri said that this would be expected with the U24 mechanism. Grantees would work with their Grants Management Office on the details.

Q: By multidisciplinary, do you mean different disciplines, such as social work, physicians, nurses, educators, etc., or could it be different specialists within a discipline, such as specialists in different branches of gastroenterology?

A: Dr. King explained that the description of the scope in the RFA refers to a range of scientific fields of inquiry, including social, behavioral, psychological, biological, and neurobiological sciences. We expect that applications will involve multiple fields such as these.

Q: Is an international proposal possible, such as one involving the United States and France?

A: Dr. McKlveen explained that foreign components such as collaborators are allowed. In general, NCCIH support of investigator-initiated clinical trials that study an intervention delivered to human subjects will be limited to studies carried out within the United States and Canada, except in special settings. For more information please see: https://nccih.nih.gov/grants/internationalclinicaltrials.

ADDITIONAL QUESTIONS SUBMITTED AFTER THE WEBINAR ENDED

Q: Given the emerging limits and reductions on university staff due to COVID-19, are there any plans for modified deadlines for this mechanism?

A: Dr. McKlveen explained that NCCIH does not have the authority to accept any applications late. The decision to accept an application late is made by the Division of Receipt and Referral (DRR) at the Center for Scientific Review (CSR). NIH has issued a policy related to the COVID-19 public health emergency. The policy states:

"When delays occur because the applicant or recipient organization is officially closed or unable to submit grant applications due to the effects of COVID-19, the NIH will consider accepting applications late, on a case-by-case basis, in accordance with the NIH Grants Policy Statement, Section 2.3.9, under the following circumstances:

- Institutions must submit applications or reports as soon as possible after reopening or resuming operations so that grant applications can be submitted, not to exceed the number of days the institution was officially closed or unable to submit grant applications.
- Institutions must submit a cover letter with the applications with enough detail about the delay so that NIH staff can make a determination whether circumstances justify accepting the application late.
- Institutions need not request advance permission to submit late due to this declared emergency.

NIH will be issuing additional guidance related to this public health emergency in the near future."

We also encourage applicants to monitor the following webpage for guidance: https://grants.nih.gov/grants/natural_disasters/corona-virus.htm

The policy can be found at:

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-20-082.html

Q: What is a U24 funding mechanism? How is a U24 different from an R24?

A: The R24/U24 mechanism can be used for a variety of purposes, so there is no one size fits all. The difference between and R and a U is that a U is a cooperative agreement and involves substantial NIH programmatic involvement with the awardees during the performance of the activities to make sure that the initiative meets the stated goals.

Some R24/U24 projects serve as coordinating centers or resource centers for larger initiatives. Others serve as hubs for innovation in a specified field, serving the broader scientific community. We are using the U24 mechanism in this latter sense, to foster activities and develop resources that will serve the field at large. The R/U24 is a flexible mechanism that permits a range of activities and affords the flexibility to respond to emerging needs as the project develops.

Each of our U24s will be a semi-independent hub for innovation in some area of well-being science. Each will have a PD and an NIH Project Scientist. There will be an expectation and a plan for us to coordinate activities across the network so that there is sharing of information, collaboration as appropriate, and opportunities to benefit from one another's advances and avoid duplication.

Q: What is the difference between a U24 and an R01?

A: An R01 is for a research project. It typically only involves the key personnel, who are conducting activities to achieve a set of specific scientific aims. The U24 is intended to support a broad research network that, though its activities, will help advance the field at large in key areas of need. The network key personnel and support staff will orchestrate a suite of activities that will likely involve others in the broader field via a range of touchpoints – as participants in workshops, as recipients of pilot funding, as consultants for specific workgroups, as trainees, as users of resources, ….

Q: How many Institutes should I collaborate with on a U24 application? Are small teams encouraged to apply, or are larger teams recommended for this opportunity?

A: The scope should be appropriate to the work proposed, which includes being able to disseminate findings to the field at large. Our sense is that rarely is the expertise necessary to develop a field found at a single institution. When we have received this question in consultations, our response has generally been that it would be important to bring together intellectual expertise across more than one institution to guide the development and implementation of network activities.

From the FOA: "The networking, education, and infrastructure-building activities required for these efforts are rarely covered under an individual grant and often do not fit the timelines for typical support mechanisms. In many instances the researchers who can support a successful network in an emerging area span multiple disciplines and are not located at a single institution. Therefore, this FOA is designed to provide research resources that create opportunities to shape the direction of an emerging field by addressing network and infrastructure development.

Applicants are strongly encouraged to limit the number of key personnel on network applications, to avoid establishing conflicts of interest throughout the emerging field. Instead, please describe the types of expertise that will be sought. Participation in network activities, including presentation at workshops, serving as faculty on summer institutes, or receiving pilot funding, will not constitute formal collaboration from the perspective of NIH, except for those key personnel listed on the application.

Network activities are intended to advance the field at large. An important consideration in developing a network is the potential to grow the field substantially through recruitment of new investigators rather than just sustaining the original team.

For network activities that span multiple institutions, applicants must propose how those activities will be coordinated across institutions, and how the proposed activities will effectively engage with other relevant activities at participating institutions."

Q: Do we have to provide detailed information about the pilot studies?

A: You must plan to have pilots but specific details about each are not required. The application must include a description of how pilots will be solicited and evaluated, in line with network priorities (See links above for examples of networks submitted in response to similar RFAs). In addition, you can include some sample pilot ideas.

Q: How many pilots should we budget for?

A: It should be based on need. Some networks have some workshops/meetings first to figure out the need, then launch a pilot competition based on priorities. Others just aim to stimulate activity and do a broad call every year. Some do or commission internal pilot work based on needs identified by the team, a review or some analyses of existing data that need to be done before a next step can be taken. It varies.

Conclusion

Ms. McRae-Williams thanked the webinar panelists and cautioned attendees to send further questions to the contacts listed in the RFA, not to the webinar mailbox, which will not be monitored.