Resource Center for Cannabis and Cannabinoid Research (U24 Clinical Trial Not Allowed) Technical Assistance Webinar (RFA-AT-24-006)

Purpose of the Webinar

On Thursday, January 25, 2024, the National Center for Complementary and Integrative Health (NCCIH) hosted a technical assistance webinar to share information about the notice of funding opportunity (NOFO) RFA-AT-24-006: Resource Center for Cannabis and Cannabinoid Research (U24 Clinical Trial Not Allowed), which is supported by NCCIH and three National Institutes of Health (NIH) partners: the National Institute on Drug Abuse (NIDA), the National Cancer Institute (NCI), and the National Institute on Aging (NIA).

Webinar Speakers

- Patrick Still, Ph.D., Program Director, Basic and Mechanistic Research Branch, Division of Extramural Research, NCCIH
- Marta Hamity, Ph.D., Scientific Review Officer, Office of Scientific Review, Division of Extramural Activities, NCCIH
- Anita McRae-Williams, M.A., Outreach Communications Program Manager, Division of Extramural Research, NCCIH (webinar moderator)

Additional NIH Staff Participating in the Q&A Session

- Heather Kimmel, Ph.D., Health Scientist Administrator, NIDA
- Kate Castro, R.N., M.S., AOCN, Program Director, Healthcare Delivery Research Program, NCI
- Devon Oskvig, Ph.D., Program Director, Division of Neuroscience, NIA

Ms. McRae-Williams welcomed the webinar participants. She explained that the webinar would be an hour long, with the first half devoted to presentations by program and review staff and the second half devoted to answering questions from webinar participants. Participants will receive the speakers' slides and a brief survey by email after the webinar ends. They will be sent a detailed written summary of the webinar within 7 or 8 days. Attendance at this webinar is optional and not a requirement for application submission.

Program Perspective

Dr. Still explained that this funding opportunity, which uses the U24 cooperative agreement funding mechanism, will support the development and maintenance of a resource to address challenges and barriers to conducting research on cannabis and its constituents, to enable researchers to successfully generate more rigorous evidence across a variety of domains in both basic and clinical research.

Significant changes have taken place in the policy landscape surrounding cannabis legalization, production, and use. But despite these changes, evidence regarding the short- and long-term health effects of cannabis remains elusive. Research conclusions often have not been appropriately synthesized, translated for, or communicated to policymakers and other stakeholders. The National Academies of Science, Engineering, and Medicine report, *The Health Effects of Cannabis and Cannabinoids*, provides a

comprehensive review of scientific evidence related to the health effects and potential therapeutic benefits of cannabis.

Dr. Still showed a slide on NIH efforts to leverage the therapeutic opportunities associated with cannabis, which include multiple funding opportunities, a 2020 NCCIH workshop, "Exploring the Mechanisms Underlying Analgesic Properties of Minor Cannabinoids and Terpenes," and an NIH-wide cannabis/cannabinoid research NOFO webpage. On June 4, 2024, NIH will host a full-day annual principal investigator (PI) meeting on exploring the mechanisms underlying analgesic properties of minor cannabinoids and terpenes. Registration for this meeting will open soon.

Response data from an August 2022 NCCIH request for information (RFI) about investigators' interests in and barriers to research on the health effects of cannabis and its constituents showed that the top needs include increased funding opportunities; increased research and clinical grade cannabis products; promotion of research standards, tools, and metrics; and providing guidance on regulatory requirements and support for early-career investigators. The NOFO discussed in today's technical assistance webinar addresses needs identified through the RFI.

Key Features of Applications in Response to This NOFO

Dr. Still explained key features of applications submitted in response to this NOFO:

- All applications must include three required core components.
- Milestones will be reviewed as part of the research strategy. Applicants must include proposed milestones for each year of requested support, including the timing and quantity of dissemination of the resource to the cannabis research community.
- Seed funds must be budgeted within the application and will be distributed as subcontracts to the third-party researcher's institution with fixed amounts.

Applications that fail to include these aspects will be considered incomplete and will not be reviewed.

The three required core components are a Regulatory Guidance Core, Research Standards Core, and Research Support Core.

Examples of needs associated with the cores include providing updates on policy changes to a centralized Center webpage (Regulatory Guidance Core), identifying and disseminating information on high-quality cannabis research products and matching specific vendors to investigators' research objectives (Research Standards Core), and organizing and convening webinars on topics that reflect Center core activities (Research Support Core).

Seed Funding Projects

The Research Support Core must budget funds for registration support and proposal development through the issuance of seed funding to the appropriate research community. Section IV of the request for applications (RFA) provides details. Seed funds are intended to support nonresearch regulatory activities to reduce barriers to future research projects in the field, in line with the stated interests of the partner NIH Institutes and Centers (ICs). For example, they could include costs for obtaining a Schedule I U.S. Drug Enforcement Administration (DEA) registration, associated equipment needed for storing and monitoring research material, or proposal development and administrative activities to conform with regulatory requirements. Seed funding projects may not exceed $50K total costs per year, regardless of

the number of awards issued. A minimum of $300K and a maximum of $400K of direct costs on average should be budgeted each year for seed funding awards (about six to eight awards per year). The selection of projects will be made in consultation with NIH staff.

Each of the participating ICs has specific priorities for seed funding. (Applicants do not need to address all these priorities.) For example:

- NIA seeks applications for seed funding that propose approaches to promote best practices to support research in diverse and understudied populations across the lifespan, including older adults and those with cognitive impairment.
- NIDA is interested in applications to promote approaches and best practices to develop and validate standard measures for evaluating cannabis and pain, substance use disorder, and comorbidities.
- NCI seeks applications to support the planning and execution of cannabis/cannabinoid clinical trials in cancer patients and survivors.
- NCCIH is interested in approaches and best practices to support research on the mechanisms by which minor cannabinoids and terpenes in the cannabis plant may affect pain pathways.

Additional Key Information

Dr. Still explained that only new applications will be accepted, clinical trials are not allowed under this NOFO, **the due date is April 16, 2024,** and late applications will not be accepted.

Review Perspective

Dr. Hamity discussed review considerations for this NOFO. Applications that are incomplete, noncompliant, or nonresponsive may not be accepted for review.

Responsiveness

Applications that are not responsive to the Scope and Responsiveness Criteria will not move forward to review. Dr. Hamity recommended looking for “must” and “need” when reading the NOFO and making sure you are responding to these requirements.

Responsive applications must include the three required core components, budget funds for the issuance of seed funding, and provide a formal plan to solicit, review, and select/prioritize requests for seed funding and evaluate the progress and outcomes of seed funding projects.

Compliance

- **Budget:** Should not exceed $850K direct cost per year. A minimum of $300K and a maximum of $400K in direct costs on average should be budgeted each year for seed fund subawards.
- **Project period:** Up to 5 years.
- **Eligibility:** Foreign components, as defined in the NIH Grants Policy Statement, are allowed. Foreign institutions and non-U.S. components of U.S. organizations are not allowed.
- **Page limitations:** Specific Aims: 1 page; Research Strategy: 12 pages.
- **Clinical trial:** Not allowed.

- **Post-submission materials:** Allowable post-submission materials are specified in NOT-OD-19-083. The due date is 30 calendar days before the peer review meeting date. **Information accidentally left out of the application cannot be provided as post-submission material.**

Completeness

Applications must include annual milestones.

Applications must comply with the instructions for Resource Sharing Plans provided in the SF424 (R&R) Application Guide.

All applications must address a Data Management and Sharing Plan (attached in the Other Plan(s) attachment in FORMS-H application forms packages).

Review Criteria

Dr. Hamity explained that the standard scored review criteria (significance, investigator[s], innovation, approach, and environment) will be used to evaluate the applications. Each of the five scored review criteria will receive a separate score, and additional review criteria will also be factored into the overall impact score. **One of the additional review criteria involves milestones.**

NOFO-specific language has been added to the standard review criteria, and the aspects of the application that reviewers are asked to assess correspond to those that applicants are asked to address in their applications. Dr. Hamity provided examples of matches between submission information requested and review criteria, taken from the NOFO. **Applicants should make sure to read and take into consideration the review criteria when preparing their applications.**

Review Panel

Applications will be reviewed in a Special Emphasis Panel at NCCIH. Reviewers will be selected based on specific areas of expertise in the target areas of the NOFO as well as clinical disciplines proposed in the applications. Reviewers will be oriented to use the additional review criteria and additional language for the standard criteria in their assessment.

Applicants should keep in mind to address how their applications would be impactful considering the goals of the funding opportunity.

Timeline

- **Letter of intent (optional):** March 16, 2024
- **Application due date:** April 16, 2024
- **Review meeting:** July 2024. The roster will be available 30 days prior to the meeting.
- **Award decision:** October 2024

Late applications will not be accepted, and the continuous submission policy does not apply.

Letters of intent should include the following information:

- Descriptive title of proposed activity
- Name, address, and telephone number of the program director(s) (PD[s])/(PI[s])

- Names of other key personnel
- Participating institutions
- Number and title of the funding opportunity

The letter should be sent to Jessica McKlveen, Ph.D., NCCIH Office of Scientific Review, at jessica.mcklveen@nih.gov.

To expedite review, applicants are asked to notify the NCCIH Referral Office by email at jessica.mcklveen@nih.gov when the application is submitted. Please include the NOFO number and title, PD/PI name, and title of the application.

Reminders

Dr. Hamity reminded participants that:

- Applications must propose and describe in detail the Center's three core components.
- The Research Support Core must budget funds for the issuance of seed funding.
- Seed funds are intended to support nonresearch regulatory activities.
- Applications must include a formal plan to solicit, review, and select/prioritize requests for seed funding, and to evaluate progress and outcomes.
- Clinical trials are not allowed.
- Letters of intent are recommended but not required.
- Applications are due April 16 by 5 p.m. local time.

Questions and Answers

Ms. McRae-Williams introduced Dr. Kimmel, Dr. Oskvig, and Ms. Castro, who joined the webinar to help answer questions.

Q: Is it expected that there will be a detailed budget by core or just an overall budget for the Center application?

A: Dr. Still explained that there is no strict allocation by core, but there are seed funding requirements in the seed funding section of the RFA.

Q: Would it be acceptable to have a coordinating core, over and above the three required cores?

A: Dr. Still said that this is acceptable. There can be an administrative core that coordinates between the three required cores. He reminded participants to make sure that, at a minimum, they include the three required core components in their applications.

Q: Our interpretation of the RFA is that seed funding is not expected until Year 2. Therefore, can the funding normally budgeted for seed funding be used for startup for Year 2?

A: Dr. Still explained that it is acceptable to "frontload" by using Year 1 seed funds for something else. Year 1 funds can be rolled over into subsequent years, or if you prefer no seed funds in Year 1, you can budget for other things, for example, the other cores. Collectively, over the 5-year period, you need to spend about $1.5 million to $2 million on seed funds, but you have flexibility on how you allocate those funds to different years.

Q: Can this award support trainees or graduate students?

A: Dr. Still said that it could, under the Research Support core, which includes convening virtual and hands-on events such as workshops and summer institutes and therefore indirectly supports trainees. Seed funds could be used for trainee support as well.

Q: Can you clarify "identify and disseminate early-career NIH reviewer opportunities"? Is the intent to educate new investigators about review processes?

A: Dr. Still said that the intent was to convey information about key NIH Center for Scientific Review study sections that the extramural community might want to look into when they submit applications. This dissemination aspect also includes workshops on grantsmanship and proposal writing. The idea is to make sure applications are aligned with the science reviewed by a particular study section of relevance to cannabinoid research and to increase communication among researchers accustomed to submitting successful applications and those who are newer to the field.

Q: Can you clarify the difference in eligibility between foreign components and non-U.S. institutions?

A: Dr. Hamity explained that foreign components are allowed. She advised checking the NIH definition of foreign components. (Please see exact definition in the NIH Grants Policy Statement.) An example of a foreign component is a collaboration with an investigator at a foreign site. However, foreign institutions or non-U.S. components of U.S. organizations are not allowed to participate in this funding opportunity.

Q: The RFA envisions that the Resource Center would interact with U.S. Food and Drug Administration (FDA) and DEA regulatory offices. Is this something the NIH project officers would do?

A: Dr. Still said that NIH would not facilitate interaction with DEA and FDA officials. This is the role of the Regulatory Guidance core. However, NIH can support and stimulate these activities as part of the cooperative agreement.

Q: What is the review process?

A: Dr. Hamity explained that once the applications are received, they will be reviewed by a Special Emphasis Panel at NCCIH. This is an in-house review. Reviewers will be selected to have the appropriate areas of expertise, based on both the funding opportunity and the science proposed in the applications. The actual review will be performed in July 2024.

Q: Does "registration support" mean DEA registration or investigational new drug (IND) registration?

A: Dr. Still said that it could be both depending on the context.

In response to a question, Ms. McRae-Williams said that the slides will be available after the webinar. She will send them to all webinar registrants. A summary of the webinar, including this Q&A, will also be sent to registrants within 7 to 8 calendar days.

Q: What are the IND issues that were on the list of NCI priorities?

A: Ms. Castro said that if a future study is going to use a new drug that is investigational, this would be the work that you need to do as background to prepare the IND application.

Q: Beyond the state-level policy of legal, medical, or decriminalized illegal categories, were any specific types of policy data mentioned as being of high interest in the RFI responses?

A: Dr. Still said that the data he showed did not have that level of granularity. To his knowledge, there was not a specific type of regulatory or policy assistance that was needed. However, in general, the community needed support in this area and suggested it as an NIH activity. Anything that can assist the community in this area would be within scope. Ms. McRae-Willliams suggested that the questioner should follow up with Dr. Still after the webinar if more detailed information is needed.

Q: Would a data and safety monitoring plan apply here given that none of the cores are explicitly collecting research data?

A: Dr. Hamity said that data and safety monitoring boards would not be required because no clinical trials will be performed.

Q: How will indirect costs associated with seed projects be handled? It appears that potential double charging of indirect costs could occur, i.e., to the award team and to the recipients of the seed grants. Will the indirect costs to seed grant recipients be included in the $300K to $400K applied each year in the grant, or will that amount be for direct costs only?

A: Dr. Still said that the Resource Center should budget at a minimum $300,000 and a maximum of $400,000 in direct costs per year on average for seed fund subawards, each of which should not exceed $50,000 in total costs. The funded Resource Center should release seed fund subawards based on fixed amounts. The awards are in the form of subcontracts to the third-party institutions. The total value of these seed fund subawards should be negotiated prior to the subawards with NIH approval, provided they meet the conditions outlined in the Grants Policy Statement: 8.1.2 Prior Approval Requirements (nih.gov). For further details, please see Section IV, Budget in RFA-AT-24-006.

Q: Is the "cannabis research community" discussed in the RFA the research community at the specific institution that is applying or does this term refer to cannabis researchers overall?

A: Dr. Still explained that it is the latter—the overall cannabis research community, not just those who are receiving the seed funds. The other cores will impact the broader community.

Q: Please confirm that pilot funds cannot be applied to clinical trials.

A: Dr. Still said that seed funds cannot be used for clinical research or research of any type but can be used for proposal development for follow-on studies and helping with regulatory issues in preparation for a clinical trial.

Q: For applicants wishing to partner with other organizations and provide seed funding for specific activities, is a list of webinar participants available?

A: Ms. McRae-Williams explained that a list of participants in this webinar will not be made available. It would have been necessary to obtain permission in advance to share participants' information, and that was not done for this event.

Q: Should all of the collaborators be physically in the same area, or would it be best to have people throughout the country?

A: Dr. Still said that having collaborators throughout the country could be beneficial. However, it is not required. The investigative team could all be at one institution or could span different institutions.

Q: Is there a Center currently established with this funding or is this a new funding opportunity?

A: This is a new funding opportunity. It builds on previous efforts of the NIH-wide cannabinoid working group, but the Resource Center as presented in the RFA is a new opportunity.

Q: Please clarify what registration support funding means.

A: Dr. Still said that, for example, seed funds could be used for fees associated with DEA registration. Seed funding can also be used for complying with regulations imposed by the DEA.

Q: What is the level of detail expected for the three core components, and what is their interaction?

A: Dr. Still said that the three cores are expected and encouraged to interact with one another. The research strategy should explain at a minimum what will be included in each core, including the objectives, expertise, milestones, and methods to achieve the core's objectives, as well as assessment of the core's impact. How this is elaborated on in each application is at the applicant's discretion.

Q: What level of description is expected for the structure and governance of the Resource Center? And how are the applicants assessed for competencies? The competencies may need to be institutional and cannot be met by letters of support.

The level of description should be sufficient to allow to reviewers to assess the structure and governance of the Resource Center as stipulated in Section V. Reviewers will be able to assess for competencies based on relevant information presented in the application, such as in the biographical sketches, the description of the institutional environment, the research strategy, and letters of support.

Q: Within 12 pages, it might be difficult to fully summarize the experience of applicants in the many key areas of the RFA. Are links to websites or publications allowed?

A: Dr. Hamity said that links cannot be included in an application.

Q: How will usability of the research center be evaluated?

A: Dr. Still explained that this will be an ongoing evaluation per the cooperative agreement, which includes evaluations by an internal advisory committee and an external advisory committee, both of which are formed in communication with the PI, study team, and NIH. At set intervals, the advisory committees evaluate how the various cores are performing and fine tune areas that can be improved.

Q: The RFA mentions a steering committee and ongoing relationship with NIH. How do you envision that relationship and how it relates to the other cores?

A: Dr. Still said that the steering committee is composed of the PI team and NIH subject matter experts. They oversee the evaluation of the Center. In that process, by default, they interact with the core PIs if necessary. This is part of the external advisory committee's evaluation, too, if there is an issue with one of the cores.

Q: For some subordinate institutions, indirect costs rates are very high, potentially reducing the amount of seed funds available to an investigator.

A: Dr. Still said that seed funds from the Center are based on fixed amounts in the form of subcontracts to the third-party institutions, where the total value of the award is negotiated upfront. The U24 recipient institution may keep the indirect costs associated with all seed fund subawards made. The Resource Center should budget at a minimum $300,000 and a maximum of $400,000 in direct cost on average for seed fund subawards. For further detail, please see Section IV, Budget in the RFA announcement.

Q: How would you recommend that applicants best collaborate with other interested organizations in submitting their application?

A: Dr. Still said that this is a central tenet of the Research Support core. They might do it, for example, through social media, annual meetings, or webinars. The creativity and innovation of this core in identifying means of dissemination of cannabis research is one of the aspects of the application that will be reviewed.

Q: Could seed funding be applied to establish the infrastructure to store cannabinoids in compliance with the DEA?

A: Dr. Still said that this is an appropriate use of seed funding.

Q: Is there a minimum number of years to provide seed funding per project? Can seed funding be awarded for 2 years, and would it be $50K per year or over the 2 years?

A: Dr. Still said that seed funding projects are $50K total costs per subaward per year.

Q: Could seed funding be applied to identify and source cannabinoids for use in clinical trials?

A: Dr. Still said this is more research oriented than the intent of the seed funding. The clinical trial itself could not be supported by seed funds. Sourcing of materials and identifying vendors is already covered within the scope of one of the cores, so it may not be appropriate for seed funding. Dr. Oskvig suggested that the individual who posed the question should follow up directly with a program official within the IC that has the best fit to their science.

Who Can Answer Your Questions?

Ms. McRae-Williams explained that NIH staff would be available to answer further questions. Before submitting an application, the best person to talk to is the program officer at the relevant IC (to discuss your ideas and plans for the project) or the scientific review officer. After submitting an application, questions should be directed to the scientific review officer. After application review, questions should be directed to the assigned program officer.

Conclusion

Ms. McRae-Williams introduced NCCIH Deputy Director Dr. David Shurtleff, who has been a pioneer in promoting this area of research. Dr. Shurtleff thanked the panel for the informative webinar. He pointed out that the use of cannabis to treat medical conditions has greatly increased without sufficient knowledge regarding the risks and benefits. More research is needed to help the public and health care providers make informed decisions. This Resource Center will be a step in the right direction to give the research community the tools they need to better study both the potential therapeutic benefits of cannabis and harms that may be associated with its use. Dr. Shurtleff said he is excited about this RFA

and looks forward to the applications that will come in. This is the beginning of greater efforts on the part of NIH to support cannabis research moving forward.

Ms. McRae-Williams thanked the panel and reminded participants that they will receive the webinar slides and summary. She encouraged participants to follow up with program staff from the participating ICs as necessary and to contact Dr. Jessica McKlveen of NCCIH for review-related questions. She then closed the webinar.