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OFFICE OF THE VICE PRESIDENT – RESEARCH AND INNOVATION

OFFICE OF THE PRESIDENT
1111 Franklin Street, 11th Floor
Oakland, California 94607-5200

Submitted through nccih.nih.gov/RFI_Cannabis and e-mailed to cannabisRFI@nih.gov

October 14, 2022

RE: UC Comments in Response to NOT-AT-22-026, "Request for Information (RFI): Investigators' Interests in and Barriers to Research Studies on the Health Effects of Cannabis and its Constituents"

Dear Sir or Madam:

I write on behalf of the University of California (UC) system with regard to the Request for Information (RFI): Investigators' Interests in and Barriers to Research Studies on the Health Effects of Cannabis and its Constituents (NOT-AT-22-026) issued on August 29, 2022.

The UC system has more than 800 research centers, institutes, laboratories, and programs that span 10 campuses, 6 medical schools, a Division of Agriculture and Natural Resources, and 3 affiliated U.S. Department of Energy national laboratories. UC has established an unparalleled reputation for first class research and innovation on a global scale and the 2nd most Nobel Prizes of any university system in the world. Specific to cannabis research, UC serves as the scientific frontrunner investigating and publishing impactful cannabis research in clinical, molecular-chemical, economic, societal, and agricultural disciplines. UC's notable cannabis research centers extend throughout the State of California:

- UC Berkeley – Cannabis Research Center
- UC Davis – Cannabis and Hemp Research Center
- UC Irvine – Center for the Study of Cannabis
- UCLA – Center for Cannabis and Cannabinoids
- UC Merced – UC Nicotine and Cannabis Policy Center
- UC Riverside – Cannabis and Hemp Agricultural Research and Regulation Center
- UC Santa Cruz – Cannabis & Hemp Initiative for Interdisciplinary Plant Studies
- UC San Francisco – Center for Tobacco Control Research and Education
- UC San Diego – Center for Medicinal Cannabis Research

As of the date of this letter, only three states in the country do not have laws that permit cannabis access in some form. Thirty-seven states and the District of Columbia allow the medical use of cannabis products. Nineteen states and the District of Columbia have enacted measures to regulate cannabis for adult non-medical use. Approved measures in 10 states allow the use of low THC, high cannabidiol (CBD) products for medical reasons in limited situations or as a legal defense. [*See*

State Medical Cannabis Laws (ncsl.org)] Despite changes in state law, substantial barriers to conducting cannabis research remain. Among these barriers are limited and singularly focused funding opportunities, a lack of a streamlined federal framework for cannabis research requirements, and limitations to only work with cannabis obtained from a federally-approved source. Provided below are further explanation of these barriers. Despite these challenges, UC researchers have made impressive strides to increase scientific knowledge around cannabis and have much to offer in expertise and experience.

1. **Cannabinoid/cannabis-related research topics of interest/importance**

UC conducts a broad range of cannabis and cannabinoid research, and currently has nine dedicated cannabis research centers. To name a few public health and safety related efforts, UC researchers have conducted clinical trials on the effect of cannabis and cannabinoids on various aspects of health, examined cannabis' role in either reducing or exacerbating opioid epidemic, looked at ways to detect cannabis intoxication in motor vehicle drivers, evaluated the health impact of new cannabis products on pregnant women and adolescents, and studied the effects of second-hand and third-hand cannabis smoke. This is just a small drop in the bucket of important work UC has done in this field, and we look forward to continuing this work, not just for the research community, but for the public and lawmakers alike to be able to make informed decisions about cannabis. For example, there is an urgent and unmet need for knowledge regarding the short- and long-term health consequences of ecologically relevant cannabis chemovars (especially those with high concentrations of delta-9-tetrahydrocannabinol), cannabis-based products and formulations, emerging novel modes of administration. Despite the legalization of medical cannabis in the State of California in 1996, very little is known regarding the safety and efficacy of cannabis for the tens of indications for which it is approved for use across the US. Barriers to research highlighted below, along with limited funding, has resulted in a situation where medical practitioners cannot guide patients. Public policy is being shaped in the absence of evidence, and health educators lack data and resources to explain risks and potential benefits of cannabis use.

2. **Existing and desirable scientific infrastructure and capacity to conduct cannabinoid/cannabis-related research**

To foster further cannabis/cannabinoid-related research, the research community needs increased funding to advance interdisciplinary and translational work. While NIH support for cannabis studies has increased, it remains siloed and targeted to specific singular topics without sufficient funding for comprehensive studies. At a minimum, UC suggests that NIH issue more R61/R33 grants, or similar mechanisms for proof of principle studies, as well as further training grants (R25), for example, on the intersection of cannabis, cannabinoid therapeutics, and co-morbid conditions. On a larger scale, UC supports the creation of cannabis/cannabinoid-related research centers of excellence as proposed in H.R. 8540 ("designation of institutions of higher education as Centers of Excellence in Cannabis Research") as a model for this approach and with funding from NIH.

Along with this effort, we remind NIH about the importance of ensuring that funding for cannabis/cannabinoid-related research include enough support for appropriate laboratory, storage, security, analytical facilities/equipment, as well as support for personnel necessary to conduct of interdisciplinary cannabis research. With the current budget cap of $500K per year, scientifically

justified, rigorous studies with high impact are very challenging to achieve, especially given the expenses related to regulatory requirements and study drug.

3. **Barriers to initiating and conducting cannabinoid/cannabis-related research including but not limited to the Schedule I license process**

Lack of Streamlined Federal Framework for Cannabis Research Requirements

Researchers wishing to conduct cannabis research must navigate a complicated maze that involve approvals from various federal agencies including the federal Drug Enforcement Agency (DEA), Food and Drug Administration (FDA), and NIH, in addition to state and institutional approvals. The time required to prepare for and obtain required registrations and approvals is substantial, can be costly, and researchers frequently plan for at least one-year's lead time before their work can commence. A unified and comprehensive framework for conducting cannabis research is crucially needed to support researchers braving the approval maze, with streamlined processes from the various federal agencies involved in regulating the conduct of cannabis research.

Inability to Study Cannabis in All Forms and from All Available Sources

Researchers are unable to study cannabis currently available in states that have passed medical and adult use cannabis laws. This is because researchers conducting cannabis research under a Schedule I registration must obtain the marijuana from a federally-approved source. The form and content of the cannabis available through the federally-approved drug supply program reportedly has not been comparable (e.g., with respect to content/ratios of THC and CBD) to some of the cannabis that is being consumed by adults living in states that have passed cannabis use laws.

While the DEA has taken steps to process applications to license new cannabis growers, this does not address the need to study the cannabis individuals buy in their own states. Moreover, dispensary cannabis products are available in an array of forms (plant, edibles, vaping liquid, topical); the effects of these varying modes of delivery and potential interactions with additive substances (e.g., flavors) is unknown and will continue to be mystery without proper research.

4. **NIH-coordinated activities that could help expand the field of therapeutic cannabinoid/cannabis-related research**

NIH should consider establishing and leading an interagency workgroup with representatives from the DEA, FDA and other agencies that fund or regulate the conduct of cannabis research. This group should thoroughly examine the current environment for the conduct of all types of cannabis/cannabinoid-related research (e.g., basic, animal, clinical, social, and behavioral). Given that all but three states currently permit some type of medical and/or recreational use of cannabis/cannabinoid by-products [*see*, Cannabis Overview (ncsl.org)], the need to effectively and efficiently conduct cannabis/cannabinoid-related research on the products being used is vital to ensuring public health.

The workgroup should focus on identifying barriers to the conduct of cannabis/cannabinoid-related research on both potential harms and benefits of cannabis. In particular, the workgroup should be

prepared to tackle head-on the cannabis' current classification as a Schedule I controlled substance and the conduct of research that may develop evidence needed to establish the requisite medicinal uses to support re-classification. Similarly, the group also should be prepared to identify hurdles in the current regulatory regime that slow or prevent the conduct of cannabis/cannabinoid-related research and identify measures to mitigate these problems.

5. **Methods, tools, or resources needed to increase cannabinoid/cannabis-related research, particularly:**

a. Strengthening the cannabinoid/cannabis research community

To accelerate research with cannabis used by the public, UC recommends that NIH, in partnership with other federal agencies, establish a national laboratory devoted to testing and confirming the constituents of publicly available products. This effort would not only help researchers understand different cannabis products and its properties, but it would also improve the overall translatability of research.

In addition, we recommend that NIH support a pipeline of diverse, well-trained researchers who can help advance cannabis-related research. In practice, this means opportunities for cross-training researchers, providing robust training grants, and the development of a coordinating center to help enhance sharing of resources across universities/centers. Models for career enhancement from other research areas (e.g., tobacco regulatory science, crop sciences) can be used to advance ways to increase capacity for the research community.

b. Guidance and assistance on regulatory requirements

Resources such as the DEA Researcher Manual and NIDA Drug Supply Program Ordering Guidelines are useful aids to assist research personnel in determining agency requirements. However, the conduct of cannabis/cannabinoid-related research frequently involves consideration of multiple agencies' regulations, including the interplay between state and federal requirements. NIH could greatly assist researchers in navigating their regulatory obligations by developing resources and training that address all sources of federal requirements and instructions on how to fulfill them. Samples of completed forms, diagrams of registration/approval processes, and answers to frequently asked questions would be especially helpful. Similarly, development of a resource page for state regulations governing research using cannabis and other Schedule I Controlled Substances (perhaps along the lines of OHRP's International Compilation of Human Research Standards) would be tremendously helpful.

Finally, researchers often encounter difficulty in obtaining agency guidance on interpretation and application of regulations, and guidance may differ across units or personnel working within an agency. NIH should establish resources to answer questions and provide institutional research personnel with prompt, consistent advice and guidance regarding agency requirements and encourage DEA and FDA to do the same.

c. Funding for regulatory compliance activities

The current annual registration fee for an individual researcher is not overly expensive but associated institutional costs can mount because each researcher is required to have an individual registration and separate registration is required for each geographic location at which controlled substances are used. In addition to registration costs, costs associated with addressing physical and administrative security requirements (e.g., narcotics safes, facility security measures, background checks for personnel, training, reverse distribution costs, etc.) are considerable. Any researcher who does not have unrestricted funding from their university must figure out ways to support the costs associated with a Schedule I storage facility and security. NIH should ensure that research funding is available for these compliance costs, especially for early investigators in order to broaden the field and improve inclusivity.

d. Research reagents such as marijuana varieties, strains, constituent chemotypes, or specific cannabinoids

As noted above, the cannabis currently available to researchers supply, however, differs substantially from the types and THC content of marijuana that is commercially available. While the NIDA Drug Supply Program is able to offer about 30% of known phytocannabinoids, the rest have to be made by researchers to evaluate their properties. Basic research with cannabinoids also involves the preparation of certain analogs and metabolites, which are also regulated and currently inaccessible. Action to improve researcher access to affordable commercially available cannabis products, or those that are at most ecologically relevant, and the ability to study various cannabis preparations is critical to evaluate public health impacts, as well as both therapeutic and negative effects.

e. Standard, validated measures of use/exposure and recommended research procedures

No comments.

f. Information sharing

UC asks that NIH support and fund the development of a cannabis research coordinating center that serves as a repository for information about research findings, career advancement, training opportunities, and funding announcements. Such an effort would enhance and accelerate research and information dissemination.

6. Access to cannabis-related information (i.e., regulatory, clinical, scientific)

The data necessary to examine critical cannabis-related questions is often scattered across many sources and often without rigorous validation. A cannabis research coordinating center, such as the one mentioned above, could seek to archive existing information on cannabis and make it available to researchers upon request.

We welcome any opportunity to further discuss the comments of this letter. If you have any questions concerning our comments, please contact Agnes Balla, Research Policy Manager, at agnes.balla@ucop.edu.

Sincerely,

Deborah Motton, Ph.D.
Executive Director
Research Policy Analysis and Coordination
University of California, Office of the President