October 15, 2022

Responses submitted via webform
Letter submitted electronically to cannabisRFI@NIH.gov

RE: 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)

The AAMC (Association of American Medical Colleges) and COGR (Council on Governmental Relations) appreciate the opportunity to provide comments on the request for information from the National Institutes of Health (NIH) on barriers to researching the health effects of cannabis. Our associations strong support for additional federal efforts to assess the potential therapeutic uses of cannabinoid and cannabis-related (CCR) compounds.

The AAMC is a nonprofit association dedicated to improving the health of people everywhere through medical education, health care, medical research, and community collaborations. Its members comprise all 156 accredited U.S. medical schools; 14 accredited Canadian medical schools; approximately 400 teaching hospitals and health systems, including Department of Veterans Affairs medical centers; and nearly 80 academic societies. Through these institutions and organizations, the AAMC leads and serves America's medical schools and teaching hospitals and the millions of individuals across academic medicine, including more than 191,000 full-time faculty members, 95,000 medical students, 149,000 resident physicians, and 60,000 graduate students and postdoctoral researchers in the biomedical sciences. Following a 2022 merger, the Alliance of Academic Health Centers and the Alliance of Academic Health Centers International broadened the AAMC's U.S. membership and expanded its reach to international academic health centers. Learn more at aamc.org.

COGR is an association of over 200 leading research universities, affiliated medical centers, and independent research institutes. COGR concerns itself with the impact of federal regulations, policies, and practices on the performance of research conducted at its member institutions. Our members account for over 95% of all federal research awards made to the higher education community or over $60 billion in research expenditures. As the national authorities on the financial and regulatory infrastructure associated with the conduct of federally funded research and corresponding compliance requirements, COGR is committed to fostering productive relationships between the research community and federal policymakers, while advocating for innovation and change that avoid unnecessary regulatory burden.

The NIH recognizes in its request several critical roadblocks to conducting cannabis research including the "lack of necessary experience and/or information regarding Federal/state regulatory requirements […]; unforeseen costs and effort related to obtaining such Federal/state licensure; and availability of and access to appropriate cannabis and cannabis products/constituents […]." We are keenly aware of these research impediments through our constituent communities: higher education institutions and their researchers, many of whom are leading cannabis research projects.

As requested by the NIH, our collective responses have been submitted through the required webform. This letter provides additional information about our organizations, collects the responses in a single document for ease of reference, and extends NIH an invitation to discuss ways our organizations could be helpful as it takes steps to develop strategies to overcome the CCR research barriers. As we emphasize in the comments below, cannabis' status as a Class I controlled substance poses significant and often insurmountable barriers to the conduct of CCR research, including research on cannabis and cannabis-products available in states where cannabis has been legalized for medicinal and/or recreational use. We also express concerns for the administrative and compliance requirements (e.g., registration process for a Class I controlled substance) which diverts time away from conducting this critical research.

Comments Submitted via Webform:

I. Scientific Infrastructure and Capacity to Conduct Cannabinoid/Cannabis-Related Research

The type of scientific infrastructure required to conduct is tied to the substance's status as a Schedule I controlled substance. As set forth in the Drug Enforcement Administration (DEA) 2022 Researcher's Manual, cannabis is considered a Schedule I controlled substance, meaning it has "no currently accepted medical use in treatment in the United States" and thus, any research using cannabis is subject to strict DEA controls. These controls include limitations on cannabis suppliers, required registration at each separate research location, and research facility security requirements. Researchers at most institutes of higher education (IHEs) cannot obtain cannabis from dispensaries in states in which cannabis has been legalized because to do so would violate federal law and compliance with the DEA's requirements is mandated per the NIH Grants Policy Statement. As emphasized below (Item 2), while research institutions and their researchers have both the interest and capacity to conduct CCR research, these barriers significantly impede their work.

To develop and maintain adequate infrastructure to support CCR research, the NIH should support the establishment of *CCR Research Centers of Excellence* that include appropriate laboratory, storage, security, analytical facilities/equipment, and provide funding to support personnel necessary for the conduct of inter-disciplinary CCR research. We also recommend that NIH ensure that funding for CCR research encompasses expenses for necessary physical and administrative security measures, as well as personnel training on the requirements for obtaining DEA researcher registration and the procedures for the use and handling of Schedule I controlled substances.

II. Barriers to Initiating and Conducting Cannabinoid/Cannabis-Related Research

Lack of a Unified Federal Framework: The primary agencies involved in funding and regulating cannabis research — FDA, DEA, and NIH — lack a unified framework for conducting research to assess the potential therapeutic use of cannabis and cannabinoids. For example, of the $1.47 billion in NIH cannabis research dollars awarded between 2000-2018, the three largest funders were NIDA, NIAAA, and NIMH, and their priority research goals indicate a "clinical award focus on drug abuse and adverse mental health effects and not on the medicinal potential of cannabis." While "there has been an upward trend in federal funding for research examining the therapeutic use of cannabis there is an emphasis on its

negative health effects." [*The cannabidiol and marijuana research expansion act: Promotion of scientific knowledge to prevent a national health crisis, The Lancet* (10/1/22)].

Difficult Registration Processes: The registration process for a Class I controlled substance is difficult to navigate and time-consuming. Barriers include the need for researchers to ensure that they have: obtained appropriate institutional, state, and/or local approvals; fulfilled the DEA and state requirements for physical inspection; separately registered each research site; and obtained an FDA investigational new drug application for clinical research. Ultimately, this requires researchers to devote significant time towards compliance, diverting time away from conducting critical research.

Limited Access to Diverse Cannabis Strains: Under federal law researchers may only use cannabis produced by manufacturers registered with the DEA. While DEA has taken steps to expand the number of cannabis suppliers for research, only seven of thirty applicants were approved to be manufacturers, and additional time is required for DEA to assign these manufacturers a production quota. [Sacirbey, O., DEA close to allowing companies to grow cannabis for scientific research, MJBiz Daily (5/18/21); DEA Marihuana Growers Information]. Thus, despite the DEA's approval of additional cannabis growers, available varieties are not representative of those available across the U.S. because current state licensed cultivators may not legally supply their products for use in federally funded research.

III. NIH-Coordinated Activities to Expand Therapeutic Cannabinoid/Cannabis-Related Research

The NIH should establish and lead an interagency working group comprised of representatives from the DEA, FDA, and other agencies that fund or regulate CCR research. The working group should be tasked with:

- Examining the current research environment for all types of CCR research, and the need to effectively and efficiently conduct CCR research on cannabis strains and products, including those that are available to the public in states in which marijuana has been legalized.
- Developing mechanisms for diverse stakeholder engagement and input, especially in the development and review of new policies and regulations.
- Addressing current barriers preventing the conduct of CCR research, including the need for increased funding opportunities to better assess the potential harms and benefits of cannabis use.
- Examining cannabis' current classification as a Schedule I controlled substance and the impact on the conduct of CCR research.
- Examining potential funding opportunities for research on cannabis and cannabis derivatives, especially for therapeutic use (e.g., chronic pain management).
- Developing resources that catalogue federal and state laws governing research using cannabis and cannabinoid.

IV. Methods, Tools, or Resources to Increase Cannabinoid/Cannabis-Related Research

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 with understanding and complying with agency requirements. However, the conduct of CCR research often requires consideration of various agency regulations and guidance, including the interplay between state and federal requirements. As noted in Section 4, the NIH,

in conjunction with the DEA and the regulated community, should develop resources to help researchers navigate federal requirements, better fulfilling their obligations (e.g., FAQs, training materials, diagrams of the DEA registration process, sample completed forms). We also recommend the development of a publicly available compendium of state laws relevant to cannabis research, along with other Schedule I controlled substances (e.g., see OHRP's International Compilation of Human Research Standards). Additionally, the NIH should work to ensure cannabis requirements are consistently applied across its departments, centers, and institutes, and the NIH should work with the DEA and the FDA to do the same.

Funding for regulatory compliance activities

The current annual registration fee for an individual researcher is not overly expensive and some researchers may qualify for fee waivers, yet costs can accumulate for institutions with multiple researchers and research sites. Additionally, the costs associated with implementing physical and administrative security requirements are considerable (e.g., narcotics safes, facility security measures, background checks for personnel, training, reverse distribution costs). To help offset this financial burden, we recommend the NIH broaden the availability of research funding to cover associated compliance costs.

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

The NIDA Drug Supply Program provides three categories of marijuana based on percent THC content: (a) low – <1% THC; (b) medium – 1-5% THC; and (c) high – 5-10% THC. The THC of the NIDA supply, however, differs substantially from the types and THC content of marijuana that is commercially available, with research showing that certain commercially available strains have significantly higher THC content, as well as genetic differences from marijuana available via NIDA (*see*, S. Reardon, et. al., "*Cannabis used in US research differs genetically to the varieties people smoke*," Nature (May 2019). As previously noted, the NIH should take immediate steps to improve researcher access to commercially available cannabis products to better assess the therapeutic effects and public health impact.

V. Closing Comments

The AAMC and COGR are pleased to respond to the NIH's Request for Information on barriers to cannabis research and recognize the importance of establishing credible scientific evidence to assess the therapeutic use of cannabis.

The classification of cannabis as a Schedule I controlled substance creates significant legal and administrative barriers, impeding meaningful advances in cannabis and cannabinoid research. As emphasized in the comments above, we recommend the NIH take immediate steps to coordinate and streamline CCR research across the eight NIH Institutes and Centers listed in this RFI, and other federal agencies as appropriate. A more harmonized approach to CCR research would increase the collection and use of cannabis data and help to facilitate an evidence-based approach to questions concerning cannabis, including its potential for therapeutic use. The development of quality data resulting from rigorous research on a substance so widely used by the public will have important research and public health benefits including opportunities to address racial justice and social equity in cannabis and cannabinoid use. Further, these efforts would help researchers conduct clinical investigations with cannabis without fear of being subject to potential sanctions for noncompliance with federal and/or state law.

We appreciate this opportunity to engage with NIH on this important topic. To improve the feasibility of CCR research, we would also be happy to bridge partnerships with experts from our constituent community who are conducting NIH-funded cannabis research. Should you have any questions regarding the attached comments, please feel free to contact Kris West, Director, Research Ethics & Compliance, COGR at kwest@cogr.edu or Daria Grayer, Senior Lead Specialist, Science Policy and Regulations, Scientific Affairs, AAMC at dgrayer@aamc.org.

Sincerely,

Ross E. McKinney, Jr. MD
Chief Scientific Officer
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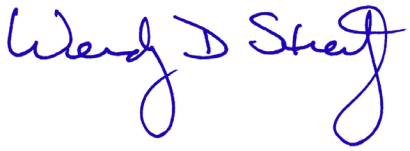

Wendy Streitz
President
COGR

cc: David J. Skorton, AAMC President and Chief Executive Officer