Subcommittee on Health
Hearing on
"Cannabis Policies for the New Decade"
January 15, 2020

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The Honorable Frank Pallone, Jr, (D-NJ)

1. **In your testimony, you discuss the therapeutic potential of cannabis to treat other health conditions. What additional evidence or types of research do we need to ensure the safety and efficacy of medical cannabis products?**

Response:
Before an intervention (e.g., a drug or other potential medical product) can be tested in people, researchers perform laboratory and animal tests to discover how the drug works and whether it is likely to be safe and work well in humans. Next, a series of clinical trials is performed to assess whether the intervention is safe when used to treat a disease and whether it provides a real health benefit. In Phase I trials, researchers test an intervention in a small group of people (20–80) for the first time to learn about its safety and identify any side effects. In Phase II trials, the intervention is given to a larger group of people (100–300) to determine its effectiveness and to further study its safety. In Phase III trials, the intervention is given to large groups of people (1,000–3,000) to confirm its effectiveness, monitor side effects, compare it with standard or similar treatments, and collect information that will allow it to be used safely. As with any drug approved by the U.S. Food and Drug Administration (FDA), any medical cannabis product would have to be tested in similar ways. We refer you to the FDA for more information on the medical product approval process.

2. **What do we know about the health consequences of cannabis arrests and convictions today and what has your agency done to promote research around the health consequences of cannabis arrests and convictions?**

Response:
Involvement with the criminal justice system is often associated with poor health outcomes. Studies have shown that having been formerly incarcerated is associated with poor mental health and physical health outcomes, as well as elevated mortality risk.[1] Social isolation, which may occur during or after incarceration, is known to have profound consequences on mental

[1] https://www.ncbi.nlm.nih.gov/pubmed/28402828

health[2] and increase the chance of future substance use.[3] It also can lead to disparities in access to effective, continuing healthcare.[4] NIDA supports research to understand how cannabis policies affect cannabis use and cannabis use disorder, arrests, and incarceration, including disparities in adolescent marijuana arrests and use.

3. **What ways is NIDA advancing research on various CBD products that consumers use?**

Response:

In Fiscal Year 2019, NIH spent $189 million on cannabinoid research, including $31 million in research on cannabidiol (CBD). NIH has a long history of supporting observational studies of individuals who use CBD and other cannabinoids to understand the health effects of such substances, to characterize patterns of use, and to understand whether individuals are using them to substitute for other drugs. In addition, NIH has been able to support research on CBD products produced by DEA-registered manufacturers, including those produced under contract with NIDA, FDA-approved cannabidiol drug products (i.e., Epidiolex), and CBD products imported into the United States with authorization from the DEA. Results from NIH-supported research contributed to the development of Epidiolex, the first FDA-approved CBD therapy, which is used to treat rare pediatric seizure disorders. NIH is also supporting research to examine CBD as a potential therapy for neuropathic pain, arthritis pain, anxiety, other seizure disorders, inflammation, digestive disorders, and opioid addiction.

With the passage of the 2018 Farm Bill, cannabis and cannabis derivatives containing no more than 0.3% delta-9 THC on a dry weight basis are considered "hemp" and are no longer regulated as controlled substances under the Controlled Substances Act. The 2018 Farm Bill explicitly preserved FDA's authority to regulate products containing cannabis or cannabis derived compounds, and at present CBD cannot be legally sold as dietary supplements or added to food. In addition, products containing more than 0.3% delta-9 THC by dry weight, regardless of CBD concentration, remain in Schedule I under the Controlled Substances Act, and unless they are acquired from a DEA-approved source, researchers cannot use NIH grants funds to purchase these products for research.

4. **You discuss in your testimony the therapeutic potential of cannabis and cannabis derivatives. Can you discuss how your agency is actively including underrepresented groups in this research?**

Response:
With limited exceptions, all NIH-funded studies that meet the NIH definition for clinical research must address plans for the inclusion of women, minorities, and individuals of all ages

[2] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5975705/
[3] https://pubmed.ncbi.nlm.nih.gov/31294075/?from_term=social+isolation+substance+use+&from_pos=6
[4] https://link.springer.com/article/10.1007%2Fs11524-018-0276-0

(as appropriate) within the grant application. Using the PHS Human Subjects and Clinical Trial Information Form, applications and proposals should include the minimum and maximum age of potential participants, describe the composition of the proposed study population in terms of sex/gender and racial/ethnic groups, and provide a rationale for selection of such subjects. Any exclusions based on sex/gender or race/ethnicity must include a rationale and justification based on a scientific or ethical basis. Investigators should also plan for appropriate outreach programs and activities to recruit and retain the proposed study population consistent with the purposes of the research project.

The Honorable Doris Matsui (D-CA)

1. **Aside from the process the Department of Justice's DEA has set up for researchers to apply for a license to be able to study cannabis, what, if any, other legal means do researchers have to study the public health effects of cannabis?**

Response:
Researchers may study the health effects of cannabis in a variety of ways that do not require having their own supply of the drug. NIH has a long history of supporting observational studies of individuals who use cannabis to understand the health effects of such substances, to characterize patterns of use, and to understand whether individuals are using them to substitute for other drugs. Such studies may include behavioral and psychological screenings, brain imaging, and other assessments to understand health. For example, NIDA, along with other NIH Institutes, Centers, and Offices, supports the Adolescent Brain Cognitive Development (ABCD) Study, a longitudinal study involving nearly 12,000 adolescents that is examining the impact of substance use, including marijuana use, and other childhood experiences on health and brain development. ABCD and studies like it often rely on an participant's self-reported use and may be limited in their capacity to definitively characterize the products participants are using, which can affect the interpretation of the results. NIH has also supported a robust portfolio of research aimed at understanding how cannabis policies affect health and other outcomes. Indeed, NIH is currently funding studies examining the relationship between cannabis policies and: cannabis and other substance use, misuse, and substance use disorders; opioid prescribing and overdose; racial disparities in cannabis-related arrests; intergenerational transmission of drug use; and other health and economic outcomes. Studies are also examining youth exposure to traditional and social media cannabis promotions and ads.

2. **How are federal agencies, and specifically the DEA, currently viewing the applicability of regulations regarding "controlled substances analogues" to synthetically derived non-psychoactive cannabinoids?**

Response:

We refer you to the DEA for the applicability of controlled substance regulations and the analogue provisions of the Controlled Substances Act to synthetically derived non-psychoactive cannabinoids.

3. **What is the position of your agency about the current status of CBD? Does the agency believe there is a distinction between marijuana-derived CBD, which is treated as a Schedule I substance, and hemp-derived and maybe even synthetically-derived CBD which is not a controlled substance? Or, alternatively, do they believe there is federal agency support for an interpretation that any CBD that has less than 0.3% THC is hemp and therefore not regulated as a controlled substance?**

Response:
It is our understanding that any cannabidiol (CBD) preparation derived from cannabis that contains no more than 0.3% delta-9 THC on a dry weight basis is hemp and is, therefore, not regulated as a controlled substance. On August 26, 2019, the DEA issued a press release stating that "…as the result of a recent amendment to federal law, certain forms of cannabis no longer require DEA registration to grow or manufacture. The Agriculture Improvement Act of 2018, which was signed into law on Dec. 20, 2018, changed the definition of cannabis to exclude 'hemp'—plant material that contains 0.3 percent or less delta-9 THC on a dry weight basis. Accordingly, hemp, including hemp plants and CBD preparations at or below the 0.3 percent delta-9 THC threshold, is not a controlled substance, and a DEA registration is not required to grow or research it." The press release is available here: https://www.dea.gov/press-releases/2019/08/26/dea-announces-steps-necessary-improve-access-marijuana-research

4. **What is the position of your agency on creating some special permissions/exemptions/safe harbor provisions for researchers studying cannabis's properties so they may transport the cannabis they're studying between their various universities without running afoul of federal law?**

Response:
It is our understanding that current regulations allow for the transfer of Schedule I and Schedule II substances between DEA registrants via the use of the DEA Form 222. We refer you to the DEA for additional information.

The Honorable Robin L. Kelly (D-IL)

The World Health Organization's Expert Committee on Drug Dependence has recognized that cannabis can confer medical benefits and has recommended to the United Nations that international drug control conventions be amended to remove cannabis from the category of strictest control. More than 30 countries have already legalized medical cannabis at the

national level. Additionally, 47 U.S. states, the District of Columbia, and four U.S. territories have amended their laws to recognize the therapeutic potential of cannabis. However, there is a gap in research on the impacts of cannabis and possible medical benefits due to many restrictions as a schedule I substance. There are various organizations including Americans for Safe Access (ASA) that promote safe and legal access to cannabis for therapeutic use and research.

1. **What changes must be made to the Controlled Substances Act and/or to other aspects of our systems of evaluation and control to enable the U.S. federal government to allow for greater research on the medicinal and therapeutic value of cannabis?**

Response:

NIDA Director Dr. Nora Volkow recently addressed the United Nations Commission on Narcotic Drugs in support of the U.S.'s recommendation to remove cannabis and cannabis preparations from Schedule IV of the Single Convention. Removal from Schedule IV of the Single Convention would not change the control status of cannabis in the United States where, under the Controlled Substances Act (CSA), "marihuana" and its constituent compounds, excluding hemp, are classified as Schedule I controlled substances – defined as having no currently accepted medical use in the United States, a lack of accepted safety for use under medical supervision, and a high potential for abuse.[5] Researchers have reported that obtaining a new registration can take more than a year, that modifying a registration can also be time consuming, and that differing interpretations of the Schedule I registration requirements among local Drug Enforcement Agency (DEA) field offices, research institutions, as well as distinct federal and state registration requirements, greatly complicate the process.

It would be useful to clarify aspects of the CSA that have been sources of confusion and administrative burden for the research community, including that it is permissible for one individual to hold a Schedule I registration under which colleagues from the same institution may work even if those colleagues do not work directly for the registrant (e.g., as members of their laboratory); that registered researchers may store, administer, and work with any substances for which they hold a researcher registration at multiple practice sites on a single contiguous campus; and that if a person is registered to conduct research with a controlled substance and applies to conduct research with a second controlled substance that is in the same schedule or in a schedule with a higher numerical designation, an inspection that was performed for purposes of the existing registration shall be sufficient to support the application. Lastly, and specifically relevant to cannabis research, it would be helpful to clarify that individuals registered to conduct research with a controlled substance who need to perform limited manufacturing activities on small quantities of that substance consistent with their research protocol (for example, creating a particular dosage formulation for research purposes) are not required to obtain a separate manufacturing registration. This would be especially helpful in cases in which researchers are required to create dosage formulations in their own laboratories from cannabis products supplied through the NIDA Drug Supply Program.

[5] https://www.deadiversion.usdoj.gov/schedules/

Research with cannabis and other Schedule I substances can only be carried out with such substances obtained from registered manufacturers as required under the Controlled Substances Act (CSA) or synthesized under a federally approved protocol. The University of Mississippi is the only domestic entity currently registered with the DEA to cultivate cannabis for research purposes, which it does under a contract with NIDA. Researchers supported by NIDA and other federal agencies may not use federal funds to purchase cannabis available through state cannabis dispensaries, as that would violate Federal law. State dispensaries are not registered under the CSA and obtaining material from these dispensaries would be in violation of the CSA. Moreover, some universities have expressed reticence about allowing investigators to purchase dispensary products with non-federal funds or do research with these products on university grounds because doing so would violate federal law. DEA has announced that it intends to review additional grower applications.. Having more than one domestic source of research cannabis would likely increase the diversity of products and formulations available to researchers, and may accelerate the development of cannabis-based medications. It should be noted, these products available to consumers have not been subjected to FDA's drug approval process.

2. **Have there been or will there be discussions between federal agency officials and their counterparts at foreign ministries in countries that dispense medical cannabis through their pharmacies to learn how they have been able to provide standardized medical cannabis to patients?**

Response:
There remains one competent authority in the United States that determines and establishes if a substance has medical use – the FDA. NIDA is a research agency, and the provision of standardized medical cannabis to patients for clinical purposes is outside of our scope. However, NIDA does support research on the therapeutic potential of cannabis, for which there is a critical need for products standards. Cannabis available through state dispensaries is grown and processed under a variety of conditions and, like other botanical products, may include pesticides, pathogenic microbes, heavy metals, and other contaminants that could be harmful to humans. While most states with legal cannabis require product testing, there is no uniform testing standard. Likewise, product labeling varies, such that it may not be possible to determine the components of a marketed product, including the full range of cannabinoids present. The lack of testing and labeling standards presents challenges to conducting controlled research with these products and poses a potential risk to users.

The Honorable Greg Walden (R-OR)

1. **What are the implications of rescheduling marijuana – say to schedule II?**

Response:

Placement of marijuana would signify a currently accepted medical use. Substances in schedule II-V have an approved medical use. HHS and DEA have reviewed multiple petitions requesting the movement of marijuana from schedule I.

The process for obtaining a Schedule II controlled substance registration is different from and involves fewer steps than the process for conducting research with Schedule I substances. The US Food and Drug Administration (FDA) Controlled Substances Program must review Schedule I research applications submitted to the U.S. Drug Enforcement Administration (DEA) for a determination of the qualifications and competency of the researcher and the merits of the protocol. For clinical research, the FDA's review is in addition to, but separate from, the review it conducts for the purposes of granting an investigational new drug (IND) approval, which is required before the DEA will issue a Schedule I registration. Moreover, each Schedule I substance the researcher is working on must be listed on the registration with authorized amounts the researcher can acquire for approved research. Changes to the protocol, including in the amount of a substance a researcher plans to use, must be reviewed by the FDA. In contrast, Schedule II-V registrations are not specific to a particular study protocol or substance (although some substances may be designated as Code H drugs, requiring additional review), and FDA's Controlled Substances Program does not review Schedule II-V registration applications.

2. **How do the current DEA registration processes for modifying a Schedule I registration to conduct research with cannabis impact the ability to do research?**

    a. **We have heard that it can take up to a year to get a Schedule I registration, and that the process of adding new cannabinoids to an existing registration and getting approval for protocol modifications is time consuming. We have also heard from the research community that differing interpretations of the registration requirements among DEA field offices as well as distinct federal and state requirements can greatly complicate the process. Can you discuss your experience and the experiences of your researchers?**

Response:

An overarching concern expressed by researchers is a lack of transparency regarding registration requirements for Schedule I and Schedule II-V substances, and differing interpretations of those requirements by DEA field agents and research institutions. In collaboration with ONDCP, HHS, FDA, and DEA, NIDA has also been identifying ways to streamline the Schedule I research registration process.

The challenges associated with conducting cannabis research, which go beyond those related to the registration process, deserve separate mention in light of the increasing availability and potency of cannabis and the proliferation of new cannabis products. Research with cannabis and other Schedule I substances can only be carried out with such substances obtained from

DEA registered sources. It would be a violation of Federal law for researchers to purchase or handle products that are being sold in dispensaries or acquired through other sources that are not Federally authorized.

The University of Mississippi is the only entity currently registered with the DEA to cultivate cannabis for research purposes, which it does under a contract with NIDA. This means that researchers supported by NIDA and other federal agencies are unable to use federal funds to purchase cannabis available through state cannabis dispensaries. Moreover, some universities have expressed reticence about allowing investigators to purchase dispensary products with non-federal funds or do research with these products on university grounds for fear of violating federal law. Having only a single source of research cannabis limits the diversity of products and formulations available to researchers and slows the development of cannabis-based medications.

3. **Some think that the best way to encourage peer-reviewed research into harms and benefits of marijuana is to completely deschedule it and all of its extracts and derivatives?**

    a. **Can we improve research without fully descheduling?**

    b. **What can be done to make it easier to research marijuana without changing its scheduling?**

Response:

Conducting research with marihuana, as defined under the Controlled Substances Act (CSA), requires a Schedule I registration from the Drug Enforcement Agency. In collaboration with ONDCP, HHS, FDA, and DEA, NIDA has also been identifying ways to streamline the Schedule I research registration process. The process of obtaining a Schedule I registration under the CSA could be improved so as to facilitate and encourage such research. Actions to address the challenges noted in response to question 2 could be helpful.

4. **I have heard frustrations from researchers about the inability to research the products sold in marijuana stores and dispensaries. For example, some of the THC vapes associated lung illnesses have been linked to licensed stores in states that have legalized recreational marijuana.**

    a. **What are some of the challenges to doing ethical research on those products?**

Response:
A significant challenge to conducting research on these products is that under federal law researchers are unable to access, for research purposes, the products that are being sold in

dispensaries or acquired through other Federally unauthorized sources. As a result, permissible research has been restricted to observational studies—or studying health outcomes in people who self-report use of these products. As such, NIH researchers have been unable to definitively characterize the products participants are using or directly test their effects in animal studies or cell cultures. Recently, however, DEA has identified a pathway for a specific program to access dispensary products for activities conducted in conjunction with law enforcement activities. This initial step may lead to additional opportunities for research on such products, including human and animal studies.

All grant applications submitted to the National Institutes of Health, including NIDA, are rigorously reviewed to assess the scientific and technical merit of the application, including the applicants' plans for the protection of human participants or research animals as appropriate. NIH requires that an institutional review board or an institutional animal care and use committee approve the research protocols used in human and animal studies, respectively. And for studies in humans, the FDA would also be required to approve an IND for studies using any THC preparation.

b. What about in animal models or in vitro?

Response:
Animal and in vitro models are often used to assess the effects of substances on a variety of systems. A wide range of physiological effects can be studied in whole animals, and effects on lung cells specifically may be assessed in vivo or in vitro. A recent publication in the New England Journal of Medicine in early 2020 described an animal model of vaping developed to study pulmonary effects of vitamin E acetate exposure.[6] Vitamin E acetate is strongly linked **to** the e-cigarette, or vaping, product use-associated lung injury (EVALI) outbreak, and this model will be a useful tool to investigate its role in this public health crisis.

5. It's my understanding that scientists looking for a diversity of product can get an import permit for schedule I substances, and research those substances from international producers. In fact, three days ago Bloomberg reported on this very issue – that medical researchers are importing marijuana products from companies outside of the US because of the insufficient supply of high quality research-grade marijuana.

a. Do you think that forcing researchers to import marijuana is better than authorizing licensed and regulated American businesses to produce federally-compliant marijuana for medical research?

Response:
The University of Mississippi is currently the only entity in the United States registered with the DEA to cultivate cannabis for research purposes, which it does under a contract with NIDA. Having only a single domestic source of research cannabis limits the diversity of products and

[6] https://www.ncbi.nlm.nih.gov/pubmed/32101656

formulations available to researchers. We were, therefore, pleased that on August 26, 2019, the DEA signaled that it is moving forward with its review of additional grower applications[7] and that it would promulgate new regulations governing cannabis cultivation.

6. **Can you describe what we currently know about the mental health effects of both casual and heavy use of marijuana?**

    a. **Is there a dose-response effect (the more you take in higher concentrations, the more the effect)?**

Response:
The association between cannabis use and mental illness is a major concern, particularly in light of the higher content of THC in today's cannabis. High doses of THC can trigger acute psychotic episodes, which is one of the main causes for emergency department visits associated with cannabis use.[8] Most of these episodes are short lasting, but some can last from days to weeks after use.[9] While overall risk of developing a lasting psychotic disorder is low, multiple studies have associated adolescent cannabis use (especially use of high potency products) with an increased overall risk for, and early onset of, chronic psychosis such as schizophrenia,[10,11] particularly in those with other risk factors.[12] Both frequent use of cannabis and use of high THC potency cannabis are associated with an increased risk of psychosis, and individuals who use high-potency products at high frequency are at even higher risk. Among patients who sought treatment for their first psychotic episode, daily cannabis users were at three times greater risk for a psychotic disorder than non-users. Daily users of high-potency cannabis were at nearly five times greater risk. Adolescent cannabis use is also associated with increased risk of suicidal behavior.[13]

Cannabis use also can lead to cannabis use disorder (CUD). Data suggest that nearly 10 percent of people who use cannabis will develop CUD.[14] People who begin using cannabis before the age of 18 are four to seven times more likely to develop CUD than adults.[15] The risks of physical dependence, addiction, and other negative consequences increase with frequent use and exposure to high concentrations of THC.[16]

[7] https://www.dea.gov/press-releases/2019/08/26/dea-announces-steps-necessary-improve-access-marijuana-research
[8] https://www.ncbi.nlm.nih.gov/pubmed/29678279
[9] https://www.ncbi.nlm.nih.gov/pubmed/31661851
[10] https://www.ncbi.nlm.nih.gov/pubmed/14754822
[11] https://www.ncbi.nlm.nih.gov/pubmed/24345517
[12] https://www.ncbi.nlm.nih.gov/pubmed/15866551
[13] https://www.ncbi.nlm.nih.gov/pubmed/15866551.
[14] https://www.ncbi.nlm.nih.gov/pubmed/26502112
[15] https://www.ncbi.nlm.nih.gov/pubmed/17888588
[16] https://www.ncbi.nlm.nih.gov/pubmed/26213314

7. **How much does the federal government spend on marijuana and cannabinoid research?**

Response:
In Fiscal Year 2019, NIH spent $189 million on cannabinoid research (which includes marijuana research), including $46 million on therapeutic cannabinoid research.[17]

   a. **Are there any private sources of funding?**

Response:
Yes, in addition to industry support for cannabis research (mostly for therapeutic applications), states also fund research on the beneficial and adverse health effects of cannabis and the effects of changes in state policies. One example is the California state-funded Center for Medicinal Cannabis Research at the University of California San Diego[18]. Non-profit organizations also support cannabis research.

   b. **Can you talk about the process for the Institute of Medicine and National Academies reports on cannabis?**

Response:
Although the report, "The Health Effects of Cannabis and Cannabinoids: The Current State of the Evidence and Recommendations for Research (2017)," was commissioned and funded by the NIH and other federal agencies, along with state agencies and non-profit groups, the report was conducted independently by the National Academies. The process for developing the report is described in detail in the report's Appendix B. We refer you to National Academies staff for additional details not available therein.

8. **Does it matter that marijuana sold today is more potent?**

Response:
NIDA data suggest that the THC concentration in commonly cultivated cannabis plants increased four-fold between 1995 and 2018 (From 4 to 16 percent in that period), and that cannabis available in dispensaries in some states has average concentrations of THC between 17.7 percent and 23.2 percent. Studies have shown that the potency of cannabis used, the frequency of use, and earlier age of onset of use all are associated with stronger negative

[17] https://report.nih.gov/categorical_spending.aspx
[18] https://www.cmcr.ucsd.edu/ , see list of publications at https://www.cmcr.ucsd.edu/index.php/publications/scientific-publications

effects.[19] Multiple studies have associated adolescent cannabis use with an overall risk for and early onset of chronic psychosis, such as schizophrenia, and both frequent use or use of high THC potency cannabis is associated with a six-fold increased risk of psychosis. Among patients who sought treatment for their first psychotic episode, daily cannabis users were at three times greater risk for a psychotic disorder than non-users. Daily users of high-potency cannabis were at nearly five times greater risk. This raises the concern that more potent cannabis might increase the risk of adverse consequences.

9. **Has your agency done any analysis on any sort of addiction concerns to CBD, including work that looks specifically at age or gender?**

Response:

Yes, NIDA has supported studies to examine the abuse liability of CBD and two recent NIDA-funded publications, published in 2016 and 2017, provide the first rigorous, controlled data on the topic. The 2016 study[20] found that CBD alone produced no significant psychoactive or cardiovascular effects and did not alter the subjective, reinforcing, or cardiovascular effects of smoked cannabis. The 2017 follow-up study[21] re-analyzed the data to examine the abuse liability for CBD alone, and found that CBD alone is no more reinforcing than a placebo control, whereas smoked cannabis reliably produced subjective reinforcing effects (e.g., ratings of being high, mellow, willing to take the drug again). A study published in 2020[22] reporting on the development of an animal model of vaporized cannabis self-administration found that vaporized THC has reinforcing properties and produces drug seeking behavior, but vaporized CBD alone does not. While these studies did not uncover any sex or age specific effects, future research may be able to build on these established results.

[19] https://pubmed.ncbi.nlm.nih.gov/26213314/
[20] https://www.ncbi.nlm.nih.gov/pubmed/26708108
[21] https://www.ncbi.nlm.nih.gov/pubmed/28088032
[22] https://www.ncbi.nlm.nih.gov/pubmed/31953372

The Honorable Gus M. Bilirakis (R-FL)

1. **Dr. Volkow – Have use patterns among cannabis users changed over time – and if so, in what ways?**

Cannabis is the most widely-used illicit drug in the country.[23] Rates of past-year use remained steady between 2002-2017, but 2018 saw an increase, with 15.9% of the population (43.5M people) reporting past-year use, a figure significantly higher than the prior 15 years. Approximately 1.6% of the population (4.4M) had a cannabis use disorder in 2018, which has remained steady since 2002. Rates of both cannabis use and use disorder are much higher among 18-25-year-olds than other age groups, and the increase in 2018 reflects increased use among 18-25-year-olds and, to a lesser degree, individuals 26 and older.

Cannabis is also the most popular illicit drug used by teens. Data from the 2019 Monitoring the Future (MTF) survey show that overall past year cannabis use rates remain steady among teens (35.7% among 12th graders; 28.8% among 10th graders; and 11.8% among eighth graders).[24] However, 2019 saw two notable increases in cannabis. First, after remaining mostly stable for many years, daily use of cannabis has increased significantly among 8th and 10th graders since 2018. In addition, past year cannabis vaping among adolescents more than doubled in the past two years: in 2019, it was 20.8% among 12th graders, 19.4% for 10th graders, and 7% for 8th graders. Past month cannabis vaping among 12th graders nearly doubled in a single year to 14% from 7.5%–the second largest one-year jump ever tracked for any substance in the history of the MTF survey. This suggests a substantial increase specifically in teens vaping cannabis.

Other modes of consuming cannabis are also increasingly available. One such method is dabbing, which involves heating and vaporizing a concentrated cannabis resin, a process that can deliver large amounts of THC to users quickly. Several studies conducted in Washington state found that sales of cannabis concentrates for vaping or dabbing have been increasing in market share as compared to cannabis flower.[25,26,27] .

   a. **Does a lack of longitudinal research on recreational use and new modes of consumption of cannabis pose a risk to public health – and if so, in what ways?**

[23] https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHNationalFindingsReport2018/NSDUHNationalFindingsReport2018.pdf
[24] https://www.drugabuse.gov/related-topics/trends-statistics/infographics/monitoring-future-2019-survey-results-overall-findings
[25] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5673542/
[26] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6948109
[27] https://pubmed.ncbi.nlm.nih.gov/31522966/

Longitudinal research on recreational use of cannabis and new modes of consumption is essential to understanding and managing the health risks of cannabis use. There is already some evidence to suggest that some modes of consumption may pose additional risks. For example, one study found that a small but disproportionate fraction of cannabis-related emergency department visits are associated with use of edible cannabis products.[1] Since these products take longer to take effect, individuals may consume more under the assumption that they did not ingest a sufficient dose the first time. This may lead to unpleasant symptoms of intense anxiety, and paranoia. Dabbing, which appears to be increasing, is notable because it exposes users to high concentrations of THC, and the use of higher potency products increases the risk of CUD, addiction, and psychosis. In addition, the outbreak of e-cigarette, or vaping, product use-associated lung injury (EVALI) is strongly linked to vitamin E acetate, an additive in some THC-containing vape products.

NIH is supporting longitudinal research to illuminate the consequences these and other products have for individual and public health. For example, the Adolescent Brain Cognitive Development (ABCD) Study will follow nearly 12,000 9- and 10-year-olds from adolescence into early adulthood, to study the effects of environmental factors, including marijuana and other drug use, on adolescent brain and cognitive development. The Population Assessment of Tobacco and Health (PATH) study, a national longitudinal study of tobacco use behavior, attitudes, and health outcomes in 49,000 people ages 12 and older, also collects data on the use of traditional nicotine delivery products, such as cigars (as blunts), hookah, and electronic devices, to consume cannabis.

b. What role do states play in cannabis-research? Do states have additional requirements for research approvals?

Some states fund cannabis research, states conduct surveillance activities to monitor cannabis related outcomes (e.g., emergency department visits), and states have their own controlled substances laws that researchers are required to follow.

c. On average, how many research solicitations for cannabis and cannabinoids are issued each year?

The NIH Guide for Grants and Contracts is NIH's official publication of notices of grant policies, guidelines and funding opportunity announcements (FOAs). Searching the guide for “cannabis,” “marijuana,” or “cannabinoid” results in 13 announcements in 2017, 22 in 2018, and 13 in 2019, for an average of 16 per fiscal year. Importantly, however, the majority of NIH-funded

[1] https://www.ncbi.nlm.nih.gov/pubmed/30721641

research is investigator-initiated, meaning that many investigators submit meritorious grant applications independent of these specific FOAs.

d. On average, what percentage of NIDA-supported research is investigating the potential medical/therapeutic uses of cannabinoids?

In fiscal year 2019, NIH supported $189 million in cannabinoid research, including $46 million in therapeutic cannabinoid research. NIDA in particular supported $118 million in cannabinoid research, including $25 million in therapeutic cannabinoid research, meaning that therapeutic cannabinoid research accounted for 1.7 percent of NIDA's $1.419 billion FY 2019 budget.[28]

2. **Dr. Volkow – 33 states and the District of Columbia have approved cannabis for medical use and 11 others along with the District of Columbia for recreational use. Several states have standards for purity and contamination, while others don't. Many organizations establish voluntary standards for a variety of products, and the use by federal agencies of voluntary consensus standards is widespread.**

a. Do you think that proactive industry efforts to develop appropriate safety standards for cannabis is a good idea – why or why not?

b. Would your agencies be willing to consider monitoring or participating in the development of these voluntary national consensus standards?

Response:
Cannabis available through state dispensaries is grown and processed under a variety of conditions and, like other botanical products, may include pesticides, pathogenic microbes, heavy metals, and other contaminants that could be harmful to humans. While most states with legal cannabis require product testing, there is no uniform testing standard. Likewise, product labeling varies, such that it may not be possible to determine the components of a marketed product, including the full range of cannabinoids present. The lack of testing and labeling standards presents health and safety concerns for users and challenges conducting controlled research with these products.

Relatedly, NIDA is soliciting input on the establishment and implementation of a standard unit of THC for cannabis research. Although not intended to serve as a safety standard for consumer products, a standard unit similar to that used for alcohol (the standard drink), tobacco (the cigarette), or opioids (morphine milligram equivalents), would improve measures of THC exposure outcomes and inform policy and public health strategies around cannabis use.

[28] https://report.nih.gov/categorical_spending.aspx