

Tab 3

NATURAL PRODUCTS

ADVERTISEMENT

Cannabis research stalled by federal inaction

US scientists face numerous barriers to studying health effects of cannabis

by **Britt E. Erickson**

JUNE 29, 2020 | APPEARED IN **VOLUME 98, ISSUE 25**

eurofins | CDMO

FIND OUT MORE



Credit: Shutterstock

Clinical researchers in the US are unable to study the safety and efficacy of cannabis products purchased from legal, state-authorized dispensaries because cannabis is illegal under federal law.

Researchers in the US who want to investigate the medical benefits and risks of cannabis are frustrated. They would like to evaluate the wide array of cannabis products sold in states where cannabis is legal, but federal law prohibits them from doing so because cannabis is still illegal at the federal level.

Most studies on the therapeutic effects of cannabis have relied on synthetic formulations of specific chemicals made by cannabis plants, such as the cannabinoids tetrahydrocannabinol (THC)—the psychoactive component of cannabis—and cannabidiol (CBD). A few researchers have looked at the efficacy of whole cannabis plants to treat chronic pain, but no clinical studies have been conducted on cannabis products purchased from state-authorized dispensaries. US researchers can only study the effects of cannabis using plant material grown by the University of Mississippi under contract with the National Institute on Drug Abuse (NIDA).

Related: Hemp growing pains

In March, the US Drug Enforcement Administration released a new rule intended to allow more organizations to grow more varieties of cannabis, but the cannabis research community says the proposal is still too restrictive. Additionally, cannabis researchers face the need to get approval from

MOST POPULAR IN BIOLOGICAL CHEMISTRY

Genetic study suggests that people's blood type may affect their COVID-19 risk

Why the best material for a homemade coronavirus face mask is hard to identify

How we know disinfectants should kill the COVID-19 coronavirus

Rethinking the role of blood pressure drugs in COVID-19

Periodic Graphics: Summer plant irritants

What do we know about the novel coronavirus's 29 proteins?

three federal agencies, and funding is limited. All these obstacles hinder cannabis research, the community says, leaving medical providers and consumers in the dark about the benefits and risks of cannabis products.

MISSISSIPPI MONOPOLY



The University of Mississippi typically harvests about 10 kg of cannabis grown indoors and about 500 kg grown outdoors—enough material to supply researchers for several years. The cannabis is ground into small particles of uniform size to be standardized for clinical research.



Credit: University of Mississippi (both)

ADVERTISEMENT

MOST POPULAR IN BIOLOGICAL CHEMISTRY

Genetic study suggests that people's blood type may affect their COVID-19 risk

Why the best material for a homemade coronavirus face mask is hard to identify

How we know disinfectants should kill the COVID-19 coronavirus

Rethinking the role of blood pressure drugs in COVID-19

Periodic Graphics: Summer plant irritants

What do we know about the novel coronavirus's 29 proteins?

ADVERTISEMENT

Researchers have complained for years about the quality and potency of the cannabis grown by the University of Mississippi. In general, it has lower levels of THC than products that are available in legal state markets, says Morgan Fox, media relations director of the National Cannabis Industry Association (NCIA), a trade group for the cannabis industry. Researchers have reported that the cannabis is moldy. Additionally, the material is “basically like powder,” Fox says. “So it is not really representative of what people are actually consuming,” he says.

The cannabis grown by the University of Mississippi has the appearance of being poor quality because it is highly processed. It is dried immediately after harvesting and stored for long periods of time, sometimes years, in a walk-in freezer at -20°C . It is also irradiated to kill off any yeasts and molds, following complaints about mold received by the US Food and Drug Administration, says Mahmoud ElSohly, a research professor who oversees the **marijuana research facility** at the University of Mississippi. Before it is shipped out to researchers, the cannabis is typically ground up into particles of uniform size.

ElSohly claims that the cannabinoids in the plant material are stable over time. “We have the appropriate stability studies” to show that, he says. But the flavor compounds in cannabis, known as terpenes, are destroyed during the drying process. Terpenes may have beneficial health effects and enhance the effects of THC and CBD. It is hard to study such effects, however, when cannabis provided for medical research doesn’t contain terpenes.

Terpenes aside, there is a good reason why cannabis grown at the University of Mississippi contains much less THC than that of cannabis sold in state dispensaries, ElSohly says. Cannabis cigarettes made for research all have to be the same size and shape, he says. When experienced cannabis users were asked to smoke a cigarette with 8% THC, they could not finish it, he says. So the highest THC content in cannabis cigarettes provided for clinical research is 6%, he notes. For comparison, cannabis sold in state dispensaries often contains as much as 30% THC.

“Our charge is not to make material similar to what is out there on the illicit market or in the state-authorized medical marijuana programs,” ElSohly says. “We are here to prepare standardized material for research that is given to all investigators so the outcome for one study can be easily compared with the outcome of another study.”

EXPANDING SOURCES, THE DEA’S WAY

The DEA acknowledges that the quality and potency of the cannabis supplied by the University of Mississippi is not representative of the cannabis that people are actually consuming in the real world. But the agency has yet to approve any of the dozens of applications from organizations who want to provide more realistic cannabis products to researchers for medical studies.

Many of those applications have been pending **since 2016**, when the DEA announced that it would adopt a new approach to increase the number of entities registered to grow cannabis for legitimate US researchers.

In **August 2019**, the DEA released the names of 33 applicants who requested to grow cannabis as bulk manufacturers for research. Many of the applicants requested approval to supply cannabis extract, which can be used in vaping products, edibles, and oral tinctures. Since then, the DEA has received a few additional applications.

The agency claims, however, that because “the size of the applicant pool is unprecedented,” it does not plan to make decisions about the applications until it changes the policies and practices that govern the bulk marijuana growers program.

The DEA provided details about those changes in the **proposed rule** released on March 23. The agency did not respond to a request from C&EN asking about the timeline for the regulation, but the process is likely to take several more months, if not years.

MOST POPULAR IN BIOLOGICAL CHEMISTRY

Genetic study suggests that people's blood type may affect their COVID-19 risk

Why the best material for a homemade coronavirus face mask is hard to identify

How we know disinfectants should kill the COVID-19 coronavirus

Rethinking the role of blood pressure drugs in COVID-19

Periodic Graphics: Summer plant irritants

What do we know about the novel coronavirus's 29 proteins?

Under the proposed rule, potential growers of cannabis for research have to satisfy a list of public interest criteria spelled out in the US Controlled Substances Act (CSA).

The criteria include having effective controls against diversion of cannabis from research to illicit uses. The DEA interprets that to mean restricting the amount grown by limiting the number of registered manufacturers “to that which can produce an adequate and uninterrupted supply of marihuana under adequately competitive conditions.” It is unclear whether the DEA will cap the number of registered manufacturers to satisfy the diversion control criteria.

ADVERTISEMENT



SPONSORED CONTENT

Multi-method characterization of responsive microgels

by Wyatt Technology Corp.

In addition, growers must have a supply agreement with a researcher who has the appropriate DEA license to study cannabis. Alternatively, growers who plan to supply cannabis for their own research purposes must register with the DEA to study cannabis and can only grow the amount authorized in their research protocol.

Potential growers also must be able to consistently produce and supply cannabis “of a high quality and defined chemical composition.” The DEA has yet to define exactly what that means. Moreover, applicants have to show “prior compliance with the CSA and DEA regulations.” It is possible that companies that have grown cannabis for state-authorized programs would be excluded from consideration because such activities are illegal under the CSA.

Besides meeting the criteria under the CSA, applicants also have to be in compliance with US obligations under an international treaty, the Single Convention on Narcotic Drugs. To meet that requirement, the DEA would take physical possession of the cannabis within 4 months of harvest and be responsible for selling the product to researchers. Growers would have to notify the DEA at least 15 days before harvest. The DEA would also have the “exclusive right of importing, exporting, wholesale trading, and maintaining stocks of cannabis and cannabis resin,” excluding cannabis-derived drugs and cannabis preparations that are regulated by the FDA, according to the proposed rule. Presumably the DEA would honor the supply contracts between growers and researchers.

“**As more states allow cannabis, the federal government still strictly controls and prohibits it, even restricting legitimate medical research.**

— *Anna G. Eshoo, chair of health subcommittee, Committee on Energy and Commerce, House of Representatives*

MOST POPULAR IN BIOLOGICAL CHEMISTRY

Genetic study suggests that people's blood type may affect their COVID-19 risk

Why the best material for a homemade coronavirus face mask is hard to identify

How we know disinfectants should kill the COVID-19 coronavirus

Rethinking the role of blood pressure drugs in COVID-19

Periodic Graphics: Summer plant irritants

What do we know about the novel coronavirus's 29 proteins?

CANNABIS COMMUNITY CONCERNS

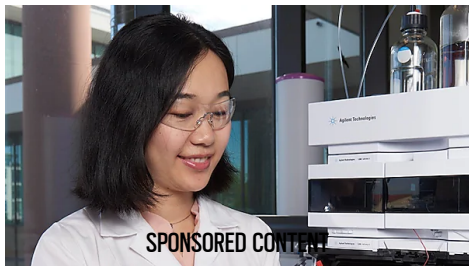
In general, the cannabis industry claims that the rule would further hinder cannabis research in the US and make it harder for organizations other than the University of Mississippi to provide cannabis to legitimate researchers.

“The DEA is not a public health or a scientific organization and has much different priorities and expertise than those organizations,” the NCIA’s Fox says. The DEA doesn’t have expertise related to facilitating research and is not in a good position to judge what research is necessary and appropriate, he notes. “So overall, we feel that they are not the appropriate agency to be charged with being the gatekeeper for research production,” he says.

The NCIA suggests that the National Institutes of Health or some other agency within the Department of Health and Human Services would be better suited to oversee cannabis produced for research.

In addition, to improve the diversity of cannabis products available to researchers, a great place to start “would be approving applications for production, particularly ones that have been sitting in the application process for up to 4 years,” Fox says. Regulators should also find “some way to allow researchers to be able to legally do research on products that are available in legal regulated cannabis markets.”

Some lawmakers agree. In comments submitted to the DEA, **Sen. Brian Schatz (D-HI)** urges the US Attorney General to waive the requirement that cannabis growers register with the DEA. Such a waiver would allow researchers with appropriate DEA licenses to obtain cannabis products from state dispensaries for research purposes.



The LC Side of "Do More with Less"

by Agilent Technologies

Researchers point to the recent outbreak of severe lung disease linked to vaping cannabis-based products to emphasize why it is important to study products that people are actually consuming. The outbreak “is extremely frightening, yet the issue cannot be effectively studied because researchers cannot work directly with cannabis products that are in actual use,” says **Theresa A. Maldonado**, vice president for research and innovation for the University of California system, in comments submitted to the DEA. She asks the DEA to allow university researchers to study cannabis products that are legally purchased from state dispensaries “without being subject to prosecution, withdrawal of

federal funds, or other sanctions.”

Related: Boom or bust ahead for cannabidiol in the US?

The University of Mississippi’s ElSohly isn’t worried about increasing the pool of growers who supply cannabis for research. “I have no problem with that,” he says. The University of Mississippi has been the sole provider of cannabis for research for more than 50 years. “It doesn’t really take away from what we are doing. It is not a competition per se, it just adds to the variety of products that are out there to be tested.” But he questions how realistic it is to test cannabis purchased from various dispensaries across the US. “Every product is going to be different,” he says.

CHANGING CRITERIA FOR GROWING CANNABIS

Growers must meet the following requirements under the Drug Enforcement Administration’s March 23 proposed rule:

- ▶ have a supply agreement with a DEA Schedule I licensed researcher or have their own license to conduct cannabis research and an authorized research protocol
- ▶ be able to consistently produce and supply high-quality cannabis
- ▶ show prior compliance with the Controlled Substances Act and DEA regulations

MOST POPULAR IN BIOLOGICAL CHEMISTRY

Genetic study suggests that people’s blood type may affect their COVID-19 risk

Why the best material for a homemade coronavirus face mask is hard to identify

How we know disinfectants should kill the COVID-19 coronavirus

Rethinking the role of blood pressure drugs in COVID-19

Periodic Graphics: Summer plant irritants

What do we know about the novel coronavirus’s 29 proteins?

- ▶ notify the DEA at least 15 days before harvest and allow the DEA to take physical possession of the cannabis within 4 months of harvest
- ▶ give the DEA exclusive rights to distribute the cannabis, including importing and exporting.

ADVERTISEMENT

RESEARCHERS TURN ELSEWHERE

As the DEA drags its feet in approving new cannabis sources for research, some university researchers have resorted to studying cannabis-based drugs imported from countries such as Canada. For example, a research group at the University of California San Diego is studying a cannabis-derived drug imported from the Canadian company Tilray to treat a movement disorder called essential tremor.

Tilray has also provided researchers at Columbia University with a cannabis-based product to test for efficacy in treating breast cancer patients suffering from taxane-induced nerve damage, a side effect of treatment with the chemotherapy drugs paclitaxel and docetaxel.

“Sourcing materials from other countries is currently pursued by NIDA in an attempt to provide more products,” says Heike Newman, a senior regulatory manager at the University of Colorado Denver who provides regulatory guidance to clinical researchers at the university who are interested in studying cannabis. “We know it is an option,” she says. “But working with these companies directly to get their products is costly and our researchers with approved funding don’t have the financial means to continue with that approach.”

“**Not everyone who is willing to participate in a clinical trial wants to smoke cannabis.**

— *Heike Newman, senior regulatory manager, University of Colorado Denver*

In addition to wanting a more varied cannabis supply, “what researchers really need are more and different formulations,” such as oral solutions or dermal products rather than rolled cigarettes, Newman says. “Not everyone who is willing to participate in a clinical trial wants to smoke cannabis,” she says. The University of Mississippi does supply two cannabis extracts, one that is high in THC and low in CBD and another that is high in CBD and low in THC, ElSohly says. Because of the growing interest in CBD oil, “we had an option to prepare 50 kg of extract,” he notes.

ADVERTISEMENT



Even so, the chorus of lawmakers calling for change is growing. Several members of Congress grilled regulators in January about the barriers to cannabis research during the first-ever cannabis **hearing** of the health subcommittee of the Committee on Energy and Commerce in the US House of Representatives.

The bulk of the hearing centered on how to resolve a dilemma that has plagued cannabis policy for decades. The DEA classifies cannabis as a Schedule I drug—a category for substances that have no medical value and high potential for abuse. Other Schedule I drugs include heroin, LSD, and ecstasy. The Schedule I classification

means that researchers must jump through all sorts of hoops, including seeking approval from three

MOST POPULAR IN BIOLOGICAL CHEMISTRY

Genetic study suggests that people's blood type may affect their COVID-19 risk

Why the best material for a homemade coronavirus face mask is hard to identify

How we know disinfectants should kill the COVID-19 coronavirus

Rethinking the role of blood pressure drugs in COVID-19

Periodic Graphics: Summer plant irritants

What do we know about the novel coronavirus's 29 proteins?

federal agencies, to study cannabis. The DEA can change how cannabis is categorized or take it off controlled substance schedules entirely if it has sufficient scientific evidence to justify the change, but researchers are impeded from doing the work that might provide such evidence because of the drug's Schedule I status.

ADVERTISEMENT

House lawmakers are considering several bills that would reschedule or deschedule cannabis. There does not appear to be broad support in Congress or within the federal government, however, to legalize cannabis at the federal level.

One possible solution to expedite medical research on cannabis is to create a subcategory of Schedule I, NIDA director Nora Volkow testified at the January hearing. NIDA has been working with the FDA and the DEA to create such a pathway, not just for marijuana but for **Schedule I substances in general**, "so that researchers don't have to go through all of the obstacles and the delayed process," she said.

Another obstacle that researchers face is extremely competitive funding for cannabis research. In fiscal 2018, the NIH funded about \$148 million on cannabinoid research, of which about \$38 million was devoted to cannabis therapeutics. The NIH prioritizes funding for cannabis therapeutic studies focused on treating pain, addiction, and inflammatory disorders, as well as for studies examining the adverse health effects of cannabis on prenatal and adolescent development.

Related: Cannabis industry gets crafty with terpenes

As the number of states legalizing cannabis for medical and adult use grows, nearly everyone agrees that more research is needed to better understand the benefits and risks.

"Thirty-three states now allow the medicinal use of cannabis and 11 states and the District of Columbia have legalized cannabis for adult use," subcommittee chair Anna G. Eshoo (D-CA) noted during the hearing. "As more states allow cannabis, the federal government still strictly controls and prohibits it, even restricting legitimate medical research."

Chemical & Engineering News
ISSN 0009-2347

Copyright © 2020 American Chemical Society

MOST POPULAR IN BIOLOGICAL CHEMISTRY

Genetic study suggests that people's blood type may affect their COVID-19 risk

Why the best material for a homemade coronavirus face mask is hard to identify

How we know disinfectants should kill the COVID-19 coronavirus

Rethinking the role of blood pressure drugs in COVID-19

Periodic Graphics: Summer plant irritants

What do we know about the novel coronavirus's 29 proteins?

YOU MIGHT ALSO LIKE...



AGRICULTURE

Hemp growing pains



CONSUMER SAFETY

Boom or bust ahead for cannabidiol in the US?



NATURAL PRODUCTS

Cannabis industry gets crafty with terpenes



SPONSORED CONTENT

The LC Side of "Do More with Less"

by Agilent Technologies

Sign up for C&EN's must-read weekly newsletter

Email Address

Subscribe »

[Contact us](#) to opt out anytime

COMMENTS

Shuki Greer

(June 30, 2020 10:39 AM)

This seems like an absurd number of requirements in order to be qualified as a cultivator for researchers. If the DEA is so intent on abiding by this 60 year old Single Convention, they should start with the MASSIVE LEGAL MARKETS AROUND THE COUNTRY!

ADVERTISEMENT

The UN isn't going to say "The US isn't following the treaty because they allow cannabis cultivation for research purposes without giving the DEA custody of the plants in time". They are going to say "The US isn't following the treaty because its freakin legal and available in 11 states across the country." This is a clear pretext on the hands of the DEA to inhibit the development of a scientific body of research that would support full cannabis legalization.

This is exactly what John Elias just testified about to the House Judiciary Committee. Both Sessions and Barr are hell-bent against marijuana like they have been watching Reefer Madness on repeat. Its a shame that our leaders aren't listening to the people. Cannabis legalization is happening already, and will not be stopped. It just might take a few baby boomers to retire before we get there.

Reply »

LEAVE A COMMENT

Name

Email*

Comments by first-time contributors will be reviewed prior to appearing on the site. This review is done by humans and not always immediately. You may be laudatory or critical, but please stay on topic and be respectful of the author and your fellow readers. We reserve the right to remove any comments that are profane, obscene, abusive, or otherwise inappropriate. Email addresses are required so that we can verify you are not a robot overlord and in case we need to contact you about your comment privately. They will not appear on the site.

Submit

*Required to comment

MOST POPULAR IN BIOLOGICAL CHEMISTRY

Genetic study suggests that people's blood type may affect their COVID-19 risk

Why the best material for a homemade coronavirus face mask is hard to identify

How we know disinfectants should kill the COVID-19 coronavirus

Rethinking the role of blood pressure drugs in COVID-19

Periodic Graphics: Summer plant irritants

What do we know about the novel coronavirus's 29 proteins?

