NO. _____

# In the Supreme Court of the United States

REV. BRYAN A. KRUMM, CNP,

*Petitioner*,

v.

U.S. DRUG ENFORCEMENT ADMINISTRATION ET AL.,

*Respondents*.

On Petition for Writ of Certiorari to the United States Court of Appeals for the District of Columbia

## PETITION FOR WRIT OF CERTIORARI

REV. BRYAN A. KRUMM, CNP
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JUNE 20, 2019

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## QUESTIONS PRESENTED

1. Can the Attorney General and DEA continue Schedule 1 placement of Cannabis now that it has "accepted medical use" in 33 States, the District of Columbia and the National Academies of Sciences?

2. Did the Court of Appeals err by granting deference to DEA's decision to limit witness testimony in spite of an ongoing pattern of witness tampering?

3. Did the Court of Appeals err by denying Krumm's Motion for Writ of Mandamus ordering the DEA to exempt Cannabis from federal control under the CSA?

## PARTIES TO THE PROCEEDING

*Petitioner*

- Rev. Bryan A. Krumm, CNP

*Respondents*

- Uttam Dillon U.S. Drug Enforcement Agency, Acting Director
- William Barr U.S. Attorney General
- Thomas B. Griffith Judge U.S. Court of Appeals for the D.C. Circuit
- Karen LeCraft Henderson Judge U.S. Court of Appeals for the D.C. Circuit
- Gregory G. Katsas Judge U.S. Court of Appeals for the D.C. Circuit

## TABLE OF CONTENTS

## TABLE OF CONTENTS – Continued

Page

## APPENDIX TABLE OF CONTENTS

## TABLE OF AUTHORITIES

Page

### CASES

## TABLE OF AUTHORITIES—Continued



## CONSTITUTIONAL PROVISIONS

## TABLE OF AUTHORITIES—Continued

## PETITION FOR WRIT OF CERTIORARI

Petitioner Rev. Bryan Krumm, CNP respectfully petitions for a writ of certiorari to review the judgment of the United States Court of Appeals for the D.C. Circuit.

## OPINIONS BELOW

On May 22, 2017 Petitioner filed a rescheduling petition with the DEA, citing a new report from the National Academies of Science (NAS) which found "There is conclusive or substantial evidence that cannabis or cannabinoids are effective for the treatment of chronic pain in adults (cannabis)." Petitioner requested that Cannabis be removed from Federal control under the CSA and that control be turned over to the States because the DEA cannot be trusted to obey the law.

On January 16, 2018 Robert Patterson, Acting administrator for the DEA denied this rescheduling petition (App.5a), claiming that the NAS review did not constitute "adequate and well controlled studies demonstrating the safety and efficacy of the drug".

On September 24, 2018 in an unpublished decision (App.1a), a three judge panel of the U.S. Court of Appeals for the D.C. circuit consisting of Judge Thomas B. Griffith, Judge Karen LeCraft Henderson, Judge Gregory G. Katsas which stated:

> ORDERED AND ADJUDGED that the petition for review be denied. Petitioner has failed to show that the Drug Enforcement Administration ("DEA") acted arbitrarily and capriciously in denying his petition to reschedule marijuana under the Controlled Substances Act, 21 U.S.C. §§ 801-971. *See Americans for Safe Access v. DEA*, 706 F.3d 438, 449 (D.C. Cir. 2013). While petitioner challenges the DEA's five-part test for determining whether a drug has a currently accepted medical use in the United States, this court has expressly approved that test. See id. Petitioner has not shown that the DEA's application of the test in this case was arbitrary and capricious. In addition, petitioner's argument that the DEA was required to engage in public notice and comment prior to denying his rescheduling petition is unavailing because neither the Controlled Substances Act nor the Administrative Procedure Act requires notice and comment prior to denying such a petition. It is FURTHER ORDERED that the motion for summary judgment be denied.

On November 2, 2018, petitioner filed a petition for rehearing en banc. On January 17, 2019, the petition for rehearing en banc was denied. (App.3a).

## STATEMENT OF JURISDICTION

The United States Court of Appeals for the D.C. Circuit denied rehearing en banc on January 17, 2019. (App.3a).This Court's jurisdiction is based upon 28 U.S.C. 1254(1) and Supreme Court Rule 10(a). Writ of Certiorari is appropriate in this case because a panel of the U.S. Court of Appeals for the District of Columbia has rendered a dramatic and unprecedented ruling that purports to override this Court's explicit determination that the States, not the federal government, determine "accepted medical use" of Cannabis. Petition for Rehearing in Banc was denied.

The Attorney General has rulemaking power to fulfill his duties under the CSA. The specific respects in which he is authorized to make rules, however, instruct us that he is not authorized to make a rule declaring illegitimate a medical standard for care and treatment of patients that is specifically authorized under state law. *Gonzales v. Oregon*, 546 U.S. 243, 258 (2006).

In this instance the DEA and Attorney General have declared that Cannabis has "no accepted medical use on the United States" while ignoring the laws of 33 States and the opinion of the NAS.

Furthermore, the Court failed to address DEA's illegal witness tampering. DEA only allows testimony from the FDA when determining if Cannabis has "accepted medical use", and then requires the FDA to only consider phase 3 clinical trials. Meanwhile, the DEA has consistently blocked these clinical trials

and demands that FDA exclude any evidence from experts in the scientific community and/or from States with Medical Cannabis Programs. By requiring that all available evidence be excluded from review, the DEA is tampering with the testimony of the FDA in order to illegally keep Cannabis in Schedule 1 of the CSA. The FDA admits that "notably, it is beyond the scope of this review to determine whether these data demonstrate that marijuana has a currently accepted medical use in the United States". (*see* Denial of Petition to Initiate Proceedings to Reschedule Marijuana, 81, Fed. Reg. 156, August 12, 2016/Proposed Rules, page 53792).

This action is timely filed because Petition for Rehearing en Banc was denied January 17, 2019.

## STATUTORY PROVISIONS

The following statutes are reproduced in the body of the petiton, *infra.*:

- 18 U.S.C. § 1512(e) (Petition p. 13)
- 21 U.S.C. § 903 (Petition p. 7)

## STATEMENT OF THE CASE

Petitioner would like to remind the Court that he is not an attorney and respectfully requests a liberal interpretation of all pleadings under *Haines v. Kerner*, 404 U.S. 519 (1972).

This case began when Krumm filed a rescheduling petition for Cannabis with the DEA December 17, 2009. After nearly 7 years of delay, on August 12, 2016, the DEA settled that petition, and although they kept cannabis listed in Schedule 1 of the CSA they were forced to adopt policies requiring them to stop blocking Cannabis research and to allow more people to grow Cannabis for research purposes. DEA was also forced to admit that Cannabis is not a "gateway drug", doesn't cause psychosis, doesn't cause lung cancer and doesn't cause cognitive impairment as you get old. When Jeff Sessions took control of the Depart of Justice he ordered the head of DEA, Chuck Rosenberg to block implementation of those policy changes. On May 22, 2017 I filed a new Rescheduling Petition requesting that Cannabis be removed from federal control, and that control be handed over to the States. This request was based on new information from the National Academies of Science which found conclusive evidence that Cannabis has proven medical value.

In September, Chuck Rosenberg resigned, stating he doesn't trust this administration to follow the law. After 6 months of delay, I sent a letter to the new head of DEA, Robert Patterson, requesting action, and January 16, 2018 he finally denied the petition. (App.5a). On February 12, 2018 I filed a Petition for Review of an Order of the United States Drug Enforcement Agency and on May 1, 2018 I filed a Petition for Writ of Mandamus to Enforce Requirements of the Controlled Substances Act, 21 U.S.C. 801 et. seq. Robert Patterson then resigned, claiming he doesn't know enough about marijuana to be in that position.

The DEA and Attorney General can't be trusted to obey the law and therefore Cannabis should be exempted from control under the CSA, with control turned over to the States to regulate Medical, Recreational, Religious and Industrial use of Cannabis. In the alternative, Cannabis must be removed from Schedule 1 of the CSA. The DEA is violating States rights by continuing Schedule 1 placement now that Cannabis has "accepted medical use" in 33 States, the District of Columbia, and the National Academy of Sciences. DEA applies a 5 part test to determine if Cannabis has "accepted medical use in the United States." As part of this test, FDA is only allowed to review phase 3 clinical trials, Meanwhile, DEA continues to ban phase 3 clinical trials of Medical Cannabis. The DEA forces the FDA to ignore the clear scientific evidence that Cannabis is safe and effective for medical use. The DEA's unreasonable, arbitrary and capricious interference with the FDA review process amounts to illegal witness tampering. These are arguments that have never been considered by this or any other court, and are deserving of review by this court in order to protect the safety and wellbeing of the American People from the illegal, unethical and immoral actions of the DEA and Attorney General.

## REASONS FOR GRANTING THE PETITION

### I. THE DECISION OF THE COURT OF APPEALS FOR THE D.C. CIRCUIT CONFLICTS WITH *GONZALES V. OREGON*, 546 U.S. 243.

This case thus sets up what may be the most important States rights cases in a generation. The DEA and Attorney General have chosen to illegally ignore the laws of 33 States and the District of Columbia. Every day the Attorney General fails to fulfill his duty to administer the CSA and order DEA to remove Cannabis from Schedule 1 of the CSA, more Americans suffer from lack of needed medication. Every day the DEA fails to do its duty to remove Cannabis from Schedule 1 of the CSA, more Americans die needlessly. Although "accepted medical use" is not defined in 21 U.S.C. § 812, it is defined in 21 U.S.C. § 903, as noted in *Gonzales v. Oregon*, 546 U.S. 243, 251 (2006), which shows that the CSA explicitly contemplates a role for the States in regulating controlled substances, as evidenced by its pre-emption provision.

> No provision of this subchapter shall be construed as indicating an intent on the part of the Congress to occupy the field in which that provision operates . . . to the exclusion of any State law on the same subject matter which would otherwise be within the authority of the State, unless there is a positive conflict between that provision . . . and that State law so that the two cannot consistently stand together.

21 U.S.C. § 903

If no state accepts the medical use of a drug or other substance, the DEA can determine whether it has accepted medical use. However, when a state accepts the medical use of a drug, the DEA is bound by that States decision. DEA relies on *Alliance for Cannabis Therapeutics v. DEA*, 15 F.3d 1131, 1135 (D.C. Cir. 1994) (approving a five part test based on scientific and medical factors) However, this was before any State had accepted the medical use of Cannabis. This decision didn't take into account the enactment of 33 State medical marijuana laws beginning in 1996. There was no conflict with State laws in 1994, because no State had accepted the medical use of Cannabis in treatment in 1994. *See*, *e.g.*, *Grinspoon v. DEA*, 828 F.2d 881, 886 (1st Cir. 1987):

We add, moreover, that the Administrator's clever argument conveniently omits any reference to the fact that the pertinent phrase in section 812(b)(1)(B) reads "in the United States," (emphasis supplied). We find this language to be further evidence that the Congress did not intend "accepted medical use in treatment in the United States" to require a finding of recognized medical use in every state or, as the Administrator contends, approval for interstate marketing of the substance.

DEA wants to read the statutory language of 21 U.S.C. § 812(b) to exclude "States" from the meaning of "in the United States" contrary to the ruling of the United States Supreme Court in *Gonzales v. Oregon*, 546 U.S. 243, 258 (2006):

> The Attorney General has rulemaking power to fulfill his duties under the CSA. The specific respects in which he is authorized to

> make rules, however, instruct us that he is not authorized to make a rule declaring illegitimate a medical standard for care and treatment of patients that is specifically authorized under state law.

DEA dictates to the States which substances shall have accepted medical use, violating Congress' mandate to regulate medical practice, not define it. DEA ignores the extensive scientific record, and boldly claims that no evidence exists regarding the medical use of Cannabis, meanwhile obscuring the fact that they've blocked that research for decades. Krumm poses a strictly legal question which does not require any extensive scientific inquiry, "does Cannabis have accepted medical use in the United States?", and the answer is clearly yes. The question of safety and efficacy was already settled in 1988 by the DEA's own administrative law judge. (*In the Matter of Marijuana Rescheduling Petition*, Docket No. 86-22, U.S. Department of Justice, Drug Enforcement Administration). The only question that remained was that of "accepted medical use". *Alliance for Cannabis Therapeutics v. DEA*, 930 F.2d 936 at 11.

> As is apparent, one salient concept distinguishing the two schedules is whether a drug has "no currently accepted medical use in treatment in the United States." This case turns on the appropriate definition and application of that phrase.

The courts have held that State laws apply in determining what constitutes accepted medical use.

> Our decision is consistent with principles of federalism that have left states as the

> primary regulators of professional conduct. *See Whalen v. Roe*, 429 U.S. 589, 603 n. 30, 51 L.Ed.2d 64, 97 S.Ct. 869 (1977) (recognizing states' broad police powers to regulate the administration of drugs by health professionals); *Linder v. United States*, 268 U.S. 5, 18, 69 L.Ed. 819, 45 S.Ct. 446 (1925) ("direct control of medical practice in the states is beyond the power of the federal government"). We must "show[] respect for the sovereign States that comprise our Federal Union. That respect imposes a duty on federal courts, whenever possible, to avoid or minimize conflict between federal and state law, particularly in situations in which the citizens of a State have chosen to serve as a laboratory in the trial of novel social and economic experiments without risk to the rest of the country." *Oakland Cannabis*, 532 U.S. at 501 (Stevens, J., concurring) (internal quotation marks omitted).

*Conant v. Walters*, 309 F.3d 629, 639 (9th Cir. 2002).

DEA's interpretation is not entitled to deference when it creates a clear violation of State sovereignty where no such conflict was intended by Congress. *Texas v. United States*, 497 F.3d 491, 500-505 (5th Cir. 2007):

> The authority of administrative agencies is constrained by the language of the statute they administer. *See Massachusetts v. EPA*, 549 U.S. 497, 127 S.Ct. 1438, 1462, 167 L.Ed. 2d 248 (2007). Under the *Chevron* doctrine, courts assess the validity of challenged

> administrative regulations by determining whether (1) a statute is ambiguous or silent concerning the scope of secretarial authority and (2) the regulations reasonably flow from the statute when viewed in context of the overall legislative framework and the policies that animated Congress's design. *See Chevron U.S.A. Inc. v. NRDC*, 467 U.S. 837, 842-43, 104 S.Ct. 2778, 2781-82 (1984).

DEA asserts that Cannabis has no accepted medical use in treatment in the United States, disregarding findings of the scientific community and with complete disdain for the Tenth Amendment. U.S. Const. amend. X. *See*, *Bond v. United States*, 564 U.S., 131 S.Ct. 2355, 2366, 180 L.Ed.2d 269, 282 (2011):

> The principles of limited national powers and state sovereignty are intertwined. While neither originates in the Tenth Amendment, both are expressed by it.

Interference with state authority to regulate in the interest of the health and welfare of its citizens is a question of constitutional law, not a scientific and medical inquiry. *Gonzales v. Oregon*, 546 U.S. 243, 270 (2006):

> [C]ongress regulates medical practice insofar as it bars doctors from using their prescription-writing powers as a means to engage in illicit drug dealing and trafficking as conventionally understood. Beyond this, however, the statute manifests no intent to regulate the practice of medicine generally. The silence is understandable given the structure and limitations of federalism, which allow the

> States "'great latitude under their police powers to legislate as to the protection of the lives, limbs, health, comfort, and quiet of all persons.'" *Medtronic, Inc. v. Lohr*, 518 U.S. 470, 475, 116 S.Ct. 2240, 135 L.Ed.2d 700 (1996) (quoting *Metropolitan Life Ins. Co. v. Massachusetts*, 471 U.S. 724, 756, 105 S.Ct. 2380, 85 L.Ed.2d 728 (1985)).

The CSA does not give the DEA administrator or the Attorney General the authority to determine whether or not a drug should be used as medicine. DEA Docket No. 86-22, 57 Fed. Reg. 10,499, 10,506 (March 26, 1992):

> Clearly, the Controlled Substances Act does not authorize the Attorney General, nor by delegation the DEA Administrator, to make the ultimate medical and policy decision as to whether a drug should be used as medicine. Instead, he is limited to determining whether others accept a drug for medical use. Any other construction would have the effect of reading the word "accepted" out of the statutory standard.

In *Gonzales v. Raich*, 545 U.S. 1 (2005), the Court wrote: "We acknowledge that evidence proffered by respondents in this case regarding the effective medical uses for marijuana, if found credible after trial, would cast serious doubt on the accuracy of the findings that require marijuana to be listed in Schedule I." *Id.* at 28 n.37. *United States v. Oakland Cannabis Buyers' Cooperative*, 532 U.S. 483 (2001), The Attorney General can include a drug in Schedule I only if the drug "has no currently accepted medical use in

treatment in the United States," "has a high potential for abuse," and has "a lack of accepted safety for use . . . under medical supervision." §§ 812(b)(1)(A)–(C). Under the statute, Cannabis can't be in Schedule 1 if it has any accepted medical use. Because Cannabis has accepted medical use by 33 States, the District of Columbia and the National Academies of Science, Cannabis must be removed from Schedule 1 of the CSA and should be removed from control of the CSA entirely.

## II. THE PANEL FAILED TO ADDRESS THE CONTINUOUS PATTERN OF ILLEGAL WITNESS TAMPERING BY DEA.

18 U.S.C. § 1512(e) states:

> In a prosecution for an offense under this section, it is an affirmative defense, as to which the defendant has the burden of proof by a preponderance of the evidence, that the conduct consisted solely of lawful conduct and that the defendant's sole intention was to encourage, induce, or cause the other person to testify truthfully.
>
> (f) For the purposes of this section—
>
> (1) an official proceeding need not be pending or about to be instituted at the time of the offense; and
>
> (2) The testimony, or the record, document, or other object need not be admissible in evidence or free of a claim of privilege.

There is nothing about the actions of the DEA to indicate that their intention has ever been to encourage, induce or cause the production a factually accurate review of Medical Cannabis. The evidence from

Krumm's previous rescheduling petition is quite clear that DEA has instituted unreasonable, arbitrary and capricious rules to manipulate the testimony of the FDA by barring them from considering the vast epidemiological proof that Cannabis is safe and effective for medical use. In the immediate case, DEA has refused to forward new evidence from the National Academies of Science to the FDA for review. This behavior proves a pattern of conspiracy to keep Cannabis illegally in Schedule 1 of the CSA, and to tamper with and/or prevent any witness testimony which might expose the illegality of Schedule 1 placement.

The Attorney General is fully complicit in these actions because he is responsible for administering the CSA and his office has ordered the DEA to violate the law by continuing to block Medical Cannabis research, and to refuse to approve new producers of Medical Cannabis, in violation of the settlement of petitioner's previous Rescheduling Petition in 2016. Because of the ongoing criminal nature of the actions of the DEA and Attorney General, they are not entitled to bar claims that could have been brought up previously. These claims show a pattern of ongoing witness tampering by the DEA and illegal conspiratorial activity between the DEA and the Attorney General, in violation of RICO laws.

DEA has ordered the FDA to adhere to irrational standards of review for Cannabis by creating rules are completely unreasonable, arbitrary, and capricious. They are an irrational abuse of authority and clear violation of Supreme Court precedent. These rules limit and control the testimony of the FDA, thus

illegally tampering with the only witness the DEA allows to provide testimony. The DEA prohibits the FDA from considering the scientific record. They ban the testimony of experts, including those at the National Academies of Sciences. They simply exclude 33 States and the District of Columbia from the definition of "in the United States". All this so they can maintain illegal placement of Cannabis in Schedule 1 of the CSA.

Krumm has proven the futility of the administrative process for moving Cannabis out of Schedule 1 of the CSA because the DEA is illegally tampering with the testimony of the FDA. Both FDA and HHS have acknowledged the futility of the administrative process as devised by DEA. In his May 20, 2015 letter to Karen DeSalvo (Acting Assistant Secretary for Health), Stephen Ostroff (Acting Commissioner of Food and Drugs) discusses 5 distinct areas of the federal regulatory system that have blocked efficient and scientifically rigorous research with marijuana and its constituents.

1. DEA has refused registration of additional cultivators of Cannabis for research.
2. PHS review is required for Cannabis research but not for other Schedule 1 substances.
3. DEA review of all research with Schedule 1 substances and registration requirements restrict research.
4. Certain Cannabis constituents have never been properly evaluated by HHS to determine if they should remain in Schedule 1.

5. DOJ/DEA and HHS need to reassess the legal and regulatory framework as applied to 1) assessment of abuse liability and 2) the assessment of currently accepted medical use for drugs that have not been approved by the FDA.

Karen DeSalvo further substantiates the futility of the administrative process in her June 3, 2015 letter to Chuck Rosenberg, when she states "Concerns have been raised about whether the existing federal regulatory system is flexible enough to respond to increased interest in research into the potential therapeutic uses of marijuana and marijuana derived drugs."

Pure THC, the primary psychoactive component of Cannabis, has long been a Schedule 3 drug. FDA has now concluded that cannabidiol (CBD) has medical use and has eased restrictions against this component of Cannabis. However, the DEA continues to insist that Cannabis has no accepted medical use. DEA simply orders the FDA to illegally ignore the vast scientific record as well as the will of 33 States and the District of Columbia, while basing their recommendation on irrational standards that are completely unreasonable, arbitrary and capricious.

In FDA's response to Krumm's previous rescheduling petition, FDA admitted that they exclude all studies of Cannabis extracts and single cannabinoids from the review. FDA then threw out dozens of studies with whole plant Cannabis and focused on 11 small studies. Although these studies proved that Cannabis was effective for treating a variety of disorders and was determined to be safe for treating

these disorders, FDA claimed there were sufficient omissions from the published reports to reject each one. The outcome of FDA's "review" was predetermined by the unreasonable, arbitrary and capricious parameters put in place by the DEA to ensure the outcome they wanted. Furthermore, DEA bars anyone else from providing evidence, or from monitoring the "review" process. Although this type of pseudoscientific approach has been used by prohibitionists for decades, it ignores reality and precludes findings of "fact".

The Data Quality Act, 44 U.S.C. § 3516 ("DQA") requires administrative agencies to develop guidelines to ensure the "quality, objectivity, utility, and integrity of information" they disseminate to the American Public. The actions of DEA, HHS, FDA, NIH and NIDA have all contributed to an ongoing campaign of misinformation which has been used to illegally maintain Schedule I placement of Cannabis in the CSA.

DEA insists that Cannabis meets none of the criteria for removal from Schedule 1 of the CSA. They have tampered with the testimony of the FDA by restricting evidence. They have consistently lied to the Courts and the American Public about the safety and efficacy of Cannabis. The most recent review from the National Academies of Science found that

> There is conclusive or substantial evidence that cannabis or cannabinoids are effective for the treatment of chronic pain in adults (cannabis), As anti-emetics in the treatment of chemotherapy induced nausea and vomiting

(oral cannabinoids) and for improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids).

*Committee on the Health Effects of Marijuana: An Evidence Review and Research Agenda*; Board on Population Health and Public Health Practice; Health and Medicine Division; National Academies of Sciences, Engineering, and Medicine; *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research* (National Academy Press 2017).

Yet DEA continues to claim "Cannabis has no accepted medical in the United States".

## CONCLUSION

For the foregoing reasons, this Court should grant Certiorari to review the decisions of the DEA and of the Court of Appeals for the D.C. circuit, in order to protect the health and welfare of the citizens of the United States.

Cannabis cannot remain in Schedule 1 of the CSA because it has "accepted medical use in the United States". Due to the futility of an administrative process, which relies solely on the decisions of federal policy makers who have demonstrated gross incompetence and/or malfeasance, the States must be allowed to fulfill their constitutional right to determine what is "accepted medical practice" within their borders. Cannabis must be removed from Schedule 1 control under the CSA and control of Cannabis

should be handed over to the States to determine how best to use it for medical, religious, and industrial and recreational purposes.

Respectfully submitted,

REV. BRYAN A. KRUMM, CNP
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JUNE 20, 2019

## APPENDIX TABLE OF CONTENTS

# JUDGMENT OF THE COURT OF APPEALS DISTRICT OF COLUMBIA (SEPTEMBER 24, 2018)

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

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BRYAN A. KRUMM, CNP,

*Petitioner*,

v.

DRUG ENFORCEMENT ADMINISTRATION,

*Respondent*.

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No. 18-1058

September Term, 2018
DEA-01/16/18 Letter

Petition for Review from an Order of the
Drug Enforcement Administration

Before: HENDERSON, GRIFFITH, and KATSAS,
Circuit Judges.

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This petition for review of an order of the Drug Enforcement Administration was considered on the briefs and the record materials filed by the parties. *See* Fed. R. App. P. 34(a)(2); D.C. Cir. Rule 34(j). Upon consideration of the foregoing and the motion for summary judgment, it is

ORDERED AND ADJUDGED that the petition for review be denied. Petitioner has failed to show that the Drug Enforcement Administration ("DEA") acted arbitrarily and capriciously in denying his petition to reschedule marijuana under the Controlled Substances Act, 21 U.S.C. §§ 801-971. *See Americans for Safe Access v. DEA*, 706 F.3d 438, 449 (D.C. Cir. 2013). While petitioner challenges the DEA's five-part test for determining whether a drug has a currently accepted medical use in the United States, this court has expressly approved that test. *See id.* Petitioner has not shown that the DEA's application of the test in this case was arbitrary and capricious. In addition, petitioner's argument that the DEA was required to engage in public notice and comment prior to denying his rescheduling petition is unavailing because neither the Controlled Substances Act nor the Administrative Procedure Act requires notice and comment prior to denying such a petition. It is

FURTHER ORDERED that the motion for summary judgment be denied.

Pursuant to D.C. Circuit Rule 36, this disposition will not be published. The Clerk is directed to withhold issuance of the mandate herein until seven days after resolution of any timely petition for rehearing or petition for rehearing *en banc*. *See* Fed. R. App. P. 41(b); D.C. Cir. Rule 41.

## ORDER OF THE COURT OF APPEALS DISTRICT OF COLUMBIA (JANUARY 17, 2019)

UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

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BRYAN A. KRUMM, CNP,

*Petitioner*,

v.

DRUG ENFORCEMENT ADMINISTRATION,

*Respondent*.

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No. 18-1058

September Term, 2018
DEA-01/16/18 Letter

Before: GARLAND, Chief Judge., and HENDERSON, ROGERS, TATEL, GRIFFITH, SRINIVASAN, MILLETT, PILLARD, WILKINS, and KATSAS, Circuit Judges.

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Upon consideration of the petition for rehearing *en banc*, and the absence of a request by any member of the court for a vote, it is

ORDERED that the petition be denied.

FOR THE COURT:

Mark J. Langer
Clerk

BY:

Ken Meadows
Deputy Clerk

## DEA ANNOUNCEMENT RELATED TO MARIJUANA AND INDUSTRIAL HEMP (NOVEMBER 8, 2016)

DEA ANNOUNCES ACTIONS RELATED TO MARIJUANA AND INDUSTRIAL HEMP

Drug Enforcement Administration
DEA Headquarters
August 11, 2016
Contact: National Media Affairs Office
Phone Number: (202) 307-7977
For Immediate Release

DEA ANNOUNCES ACTIONS RELATED TO MARIJUANA AND INDUSTRIAL HEMP

WASHINGTON-The Drug Enforcement (DEA) announced several marijuana-related actions, including actions regarding scientific research and scheduling of marijuana, as well as principles on the cultivation of industrial hemp under the Agricultural Act 012014.

**DEA Publishes Responses to Two Pending Petitions to Reschedule Marijuana-**

DEA has denied two petitions to reschedule marijuana under the Controlled Substances (CSA). In response to the petitions, DEA requested a scientific and medical evaluation and scheduling recommendation from the Department of Health and Human (HHS), which was conducted by the U.S. Food and Drug (FDA) in consultation with the National Institute on Drug (NIDA). Based on the legal standards in the CSA, marijuana remains a schedule I controlled sub-

stance because it does not meet the criteria for currently accepted medical use in treatment in the United States, there is a lack of accepted safety for its use under medical supervision, and it has a high potential for abuse.

In his letter to the petitioners, DEA Acting Administrator Chuck Rosenberg offered a detailed response outlining the factual and legal basis for the denial of the petitions.

The full responses to the petitions can be found in the Federal Register. Response 1 AND Response 2

The DEA and the FDA continue to believe that scientifically valid and well-controlled clinical trials conducted under investigational new (IND) applications are the most appropriate way to conduct research on the medicinal uses of marijuana. Furthermore, DEA and FDA believe that the drug approval process is the most appropriate way to assess whether a product derived from marijuana or its constituents is safe and effective and has an accepted medical use. This pathway allows the FDA the important ability to determine whether a product meets the FDA criteria for safety and effectiveness for approval.

## Increasing the Number of Authorized Marijuana Manufacturers Supplying Researchers

DEA announced a policy change designed to foster research by expanding the number of DEA-registered marijuana manufacturers. This change should provide researchers with a more varied and robust supply of marijuana. At present, there is only one entity authorized to produce marijuana to supply researchers in the United States: the University of

Mississippi, operating under a contract with NIDA. Consistent with the CSA and U.S. treaty obligations, DEA's new policy will allow additional entities to apply to become registered with DEA so that they may grow and distribute marijuana for FDA-authorized research purposes.

This change illustrates DEA's commitment to working together with the FDA and NIDA to facilitate research concerning marijuana and its components. DEA currently has 350 individuals registered to conduct research on marijuana and its components. Notably, DEA has approved every application for registration submitted by researchers seeking to use NIDA-supplied marijuana to conduct research that HHS determined to be scientifically meritorious.

**Statement of Principles Concerning industrial Hemp and the Agricultural Act of 2014-**

The U.S. Department of (USDA), in consultation with DEA and the FDA, also released a statement of principles concerning provisions of the Agricultural Act of 2014 relating to the cultivation of industrial hemp. Industrial hemp is a low-concentration THC variety of the cannabis plant intended to be used for industrial (*e.g.*, fiber and seed). This is intended to inform the public, including institutions of higher education and State departments of agriculture, how Federal law applies to activities associated with industrial hemp that is grown and cultivated in accordance with Section 7606 of the Agricultural Act of 2014.

This statement of principles outlines the legalized growing and cultivating of industrial hemp for research purposes under certain conditions, such as in states

where growth and cultivation are legal under state law. The 2014 Act did not remove industrial hemp from the list of controlled substances and, with certain limited exceptions, the requirements of the Federal Food, Drug, and Cosmetic Act and the CSA continue to apply to industrial hemp-related activities. The statement of principles addresses questions including the extent to which private parties may grow industrial hemp as part of an agricultural pilot program, the circumstances under which the sale of hemp products is permitted, and other related topics.

# FDA RECOMMENDATIONS ON THE SCHEDULING OF MARIJUANA UNDER THE CONTROLLED SUBSTANCES ACT (MAY 20, 2015)

DEPARTMENT OF
HEALTH & HUMAN SERVICES
Food and Drug Administration
Silver Spring, MD 20993

TO: Acting Assistant Secretary for Health

FROM: Acting Commissioner of Food and Drugs

SUBJECT: Recommendation to Maintain Marijuana in Schedule I of the Controlled Substances Act

## ACTION

Attached are the Food and Drug Administration's (FDA) scientific and medical evaluations and recommendations on the scheduling of marijuana under the Controlled Substances Act (CSA), prepared in response to two petitions submitted to the Drug Enforcement Administration (DEA). Each contains the same recommendation to maintain marijuana in Schedule 1 of the CSA.

On December 17, 2009, Mr. Bryan Krumm submitted a petition to DEA, requesting that proceedings be initiated to repeal the rules and regulations that place marijuana in Schedule I of the CSA. Mr. Krumm contends that marijuana has an accepted medical use in the United States, has proven safety and efficacy, is safe for use under medical supervision,

and does not have the abuse potential for placement in Schedule I of the CSA. In 2011, the DEA Administrator requested that the U.S. Department of Health and Human Services (HHS) provide a scientific and medical evaluation of the available information and a scheduling recommendation for marijuana, in accordance with the provisions of 21 U.S.C. 811(b).

On November 30, 2011, Governors Lincoln D. Chafee of Rhode Island and Christine a Gregoire of Washington also submitted a petition to DEA requesting that proceedings be initiated to repeal the rules and regulations that place marijuana in Schedule I-of the CSA. Specifically, they requested the reclassification of marijuana from Schedule Ito Schedule II of the CSA. The petition contends that marijuana has an accepted medical use in the United States, is safe for use under medical supervision, and has a relatively low abuse potential compared to Schedule II substances in the CSA. In June 2013, the DEA Administrator requested that HHS provide a scientific and medical evaluation of the available information and a scheduling recommendation for marijuana, in accordance with the provisions of 21 U.S.C. 811.(b).

FDA and the National Institute on Drug Abuse (NIDA) have carefully considered the available scientific and medical evidence for marijuana presented under the eight factors determinative of control under the CSA, 21 U.S.C. 811(c). Pursuant to the requests in the petitions, FDA broadly evaluated marijuana, and did not focus its evaluation on particular strains of marijuana or components or derivatives of marijuana. In the development of this scientific and medical evaluation for the purpose of scheduling, we reviewed and analyzed considerable data related to marijuana's

abuse potential. The data include the pharmacology of marijuana and its components, the prevalence and frequency of marijuana use, the widespread availability of marijuana for nonmedical use, the ease of obtaining or manufacturing marijuana, and at-risk populations including children and adolescents. In addition, we reviewed the scientific literature on whether marijuana has a currently accepted medical use, and we analyzed studies evaluating medical treatment with marijuana. Our review of the published clinical studies is also attached.

## DISCUSSION

FDA recommends that marijuana be maintained in Schedule I of the CSA. NIDA concurs with this recommendation.

Since our 2006 scientific and medical evaluation and scheduling recommendation responding to a previous DEA petition, research with marijuana has progressed. However, more research should be conducted into marijuana's effects, including potential medical uses for marijuana and its derivatives. Our review of the available evidence and the published clinical studies indicated some study design challenges that need to be addressed to ensure that future studies generate scientific data that can be used to determine whether marijuana has an accepted medical use. For example, we recommend that studies need to focus on consistent administration and reproducible dosing of marijuana, potentially through the use of administration methods other than smoking. A summary of our review of the published literature on the clinical uses of marijuana, including our recom-

mendations for future research, is attached to this document.

FDA and NIDA also believe that work continues to be needed to ensure support by the federal government for the efficient conduct of clinical research using marijuana and its derivatives. Concerns have been raised about whether the existing federal regulatory system is flexible enough to respond to increased interest in research into the potential therapeutic uses of marijuana and marijuana-derived drugs. For instance, several states have moved to facilitate marijuana research and have directly questioned whether, for instance, research marijuana may be procured from sources other than the existing single NIDA contractor.[1] The leaders of the Senate Caucus on International Narcotics Control have asserted that DEA registration "present[s] significant practical problems for researchers."[2] In addition, they stated that "it is unclear why marijuana is the only Schedule I substance for which [Public Health Service (PHS)] review and approval is required."[3]

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[1] A Colorado statute directs the state attorney general to "seek authority from the federal government to permit Colorado institutions of higher education to contract with [NIDA] to cultivate marijuana and its component parts for use" in state-funded marijuana research (C.R.S.A. § 25-1.5-106.5).

[2] Letter from Sen. Dianne Feinstein and Sen. Charles Grassley to Att'y Gen. Eric Holder, and Sec'y Sylvia M. Burwell (Oct. 20, 2014).

[3] *Id.*

### Discrete Aspects of Federal Marijuana Oversight for Potential Review

Upon examining the current federal regulatory system, FDA and NIDA note the following discrete aspects of marijuana oversight that might be reviewed by HHS or Dal/DEA, as appropriate, with the goal of promoting efficient and scientifically rigorous research with marijuana and its constituents. Interagency coordination may be necessary to ensure that any revisions to federal marijuana regulations result in an appropriate level of oversight and are consistent with treaty obligations.

#### 1. DEA registration of additional cultivators of marijuana for research

There is currently only one cultivator of marijuana that is registered with DEA for that purpose. DEA may wish to review whether, consistent with statutory requirements and any applicable treaty obligations, it may register additional cultivators of marijuana. •

#### 2. PHS review of marijuana research protocols

PHS review of research protocols is not required in order to conduct research of other substances, including research of other Schedule I substances. Many aspects of PHS review arguably duplicate FDA's review of investigational new drug (IND) applications. HHS may wish to consider whether the PHS review process is unnecessary and could be

discontinued.[4]

### 3. Registration requirements for researchers of marijuana-derived drugs

Researchers of Schedule I drugs, including marijuana and marijuana-derived drugs, must submit research protocols to be reviewed by DEA in order to become registered to conduct such research. DEA may wish to consider whether it may invoke its statutory waiver authority, under 21 USC § 822(d), to waive the registration requirement for certain researchers of marijuana or marijuana-derived drug products.[5] For instance, DEA may wish to consider whether such a waiver might be appropriate if it were subject to certain conditions, such as compliance with FDA requirements (*e.g.*, an effective IND), or by limiting the waiver's applicability to research with certain marijuana-derived constituents (*e.g.*, cannabidiol (CBD)) that may have reduced abuse potential. (An HHS analysis of the abuse potential of these constituents, as described in #4 below, may be useful to inform this decision.)

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[4] In 2014, FDA and NIDA separately endorsed dissolving the PHS committee and presented that recommendation to the Office of the Assistant Secretary for Health.

[5] 21 USC 822(d) provides: "The Attorney General may, by regulation, waive the requirement for registration of certain manufacturers, distributors, or dispensers if he finds it consistent with the public health and safety."

**4. Evaluation of the abuse potential of certain marijuana constituents**

Similar to the current "8-factor analysis" conducted for marijuana, HHS may wish to consider whether a similar evaluation conducted for CBD or other constituents of marijuana could help inform decision-making about those constituents. For example, depending on the outcome, such an evaluation could help provide a basis for a recommendation to remove those constituents from Schedule I or could support reduced restrictions on research of the constituents, such as the limited DEA registration waiver for researchers discussed in #3 above. Removal of certain marijuana constituents from Schedule I may make it easier to conduct rigorous scientific studies of those constituents to support submission of a new drug application to FDA. We note that the leaders of the Senate Caucus on International Narcotics Control have recently requested that HHS and DOJ evaluate the appropriate schedule of CBD.[6] In order to meet this request, a study of the human abuse potential of CBD would likely be needed, because sufficient information in this area is not yet available.

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[6] On May 13, 2013, the Caucus leaders requested that "HHS, in concert with DOJ, immediately evaluate the factors determinative of control or removal from [CSA] schedules for CBD, and make a scheduling recommendation for it. . . ." Letter from Sen. Dianne Feinstein and Sen. Charles Grassley to Sec'y Sylvia M. Burwell (May 13, 2015).

### 5. Reassessment of the Legal and Regulatory Framework for Marijuana Rescheduling

> NIDA points out that another potential area for review is the legal and regulatory framework applied to (1) the assessment of abuse liability for substances in Schedule I (including the comparative standard used to assess the relative risk of abuse) and (2) the assessment of currently accepted medical use for drugs that have not been approved by FDA. While potentially daunting (depending on its scope and nature), re-evaluation of the legal and regulatory framework by DOJ/DEA and HHS could identify ways to encourage appropriate scientific research into the potential therapeutic uses of marijuana and its constituents.

In summary, both FDA and NIDA believe that it is important to continue to review the federal support for research into the potential therapeutic uses of marijuana, and that there is a potential public health value in exploring options like those outlined above with a goal of promoting efficient and scientifically rigorous research.

## CONCLUSION

FDA and NIDA have evaluated the medical and scientific information available on marijuana in accordance with 21 U.S.C. § 811 (b)-(c) and recommend that the available data warrant that marijuana be maintained in Schedule I of the CSA. We recommend that these findings be conveyed to the DEA Administrator.

We have prepared, for your signature, a letter of transmittal to the DEA Administrator, which includes the necessary scientific and medical evaluation and scheduling recommendation documents in response to the two petitions/requests from DEA recommending the maintaining of marijuana in Schedule I of the CSA. We have also attached our review of the published clinical studies.

/s/ Stephen M. Ostroff
Stephen M. Ostroff, M.D.

Attachments

**DECISION**

Approved _____ Disapproved _____ Date 6/3/15

# HEALTH & HUMAN SERVICES RECOMMENDATION ON THE SCHEDULING OF MARIJUANA UNDER THE CONTROLLED SUBSTANCES ACT (JUNE 3, 2015)

DEPARTMENT OF
HEALTH & HUMAN SERVICES
Office of the Assistant Secretary for Health
Washington, D.C. 20201

The Honorable Chuck Rosenberg
Acting Administrator
Drug Enforcement Administration
U.S. Department of Justice
8701 Morrissette Drive
Springfield, VA 22152

Dear Mr. Rosenberg:

Pursuant to the Controlled Substances Act (CSA, 21 U.S.C. § 811(b), (c), and (f)), the Department of Health and Human Services (HHS) is recommending that marijuana continue to be maintained in Schedule I of the CSA.

The Food and Drug Administration (FDA) and the National Institutes of Health's National Institute on Drug Abuse (NIH/NIDA) have also considered the abuse potential and dependence-producing characteristics of marijuana.

Marijuana meets the three criteria for placing a substance in Schedule I of the CSA under 21 U.S.C. 812(b)(1). As discussed in the enclosed analyses, marijuana has a high potential for abuse, no currently

accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. Accordingly, HHS recommends that marijuana be maintained in Schedule I of the CSA. Enclosed are two documents prepared by FDA's Controlled Substance Staff (in response to petitions filed in 2009 by Mr. Bryan Krumm and in 2011 by Governors Lincoln D. Chafee and Christine O. Gregoire) that form the basis for the recommendation. Pursuant to the requests in the petitions, FDA broadly evaluated marijuana, and did not focus its evaluation on particular strains of marijuana or components or derivatives of marijuana.

FDA's Center for Drug Evaluation and Research's current review of the available evidence and the published clinical studies on marijuana demonstrated that since our 2006 scientific and medical evaluation and scheduling recommendation responding to a previous DEA petition, research with marijuana has progressed. However, the available evidence is not sufficient to determine that marijuana has an accepted medical use. Therefore, more research is needed into marijuana's effects, including potential medical uses for marijuana and its derivatives. Based on the current review, we identified several methodological challenges in the marijuana studies published in the literature. We recommend they be addressed in future clinical studies with marijuana to ensure that valid scientific data are generated in studies evaluating marijuana's safety and efficacy for therapeutic use. For example, we recommend that studies need to focus on consistent administration and reproducible dosing of marijuana, potentially through the use of administration methods other than smoking. A sum-

mary of our review of the published literature on the clinical uses of marijuana, including recommendations for future studies, is attached to this document.

FDA and NIDA also believe that work continues to be needed to ensure support by the federal government for the efficient conduct of clinical research using marijuana. Concerns have been raised about whether the existing federal regulatory system is flexible enough to respond to increased interest in research into the potential therapeutic uses of marijuana and marijuana-derived drugs. HHS welcomes an opportunity to continue to explore these concerns with DEA.

Should you have any questions regarding these recommendations, please contact Corinne P. Moody, Science Policy Analyst, Controlled Substance Staff, Center for Drug Evaluation and Research, FDA, at (301) 796-3152.

Sincerely yours,

/s/ Karen B. DeSalvo
Karen B. DeSalvo, MD, MPH, MSc
Acting Assistant Secretary for Health

Enclosures

# FEDERAL REGISTER ENTRY ON FDA REVIEW ON CLINICAL TRIALS (AUGUST 12, 2016)

Vol. 81 Friday,
No. 156 August 12, 2016
OFFICE OF THE FEDERAL REGISTER

. . . Columbia have passed state-level medical marijuana laws that allow for marijuana use within that state; similar bills are pending in other states.

The present review was undertaken by the Food and Drug Administration (FDA) to analyze the clinical studies published in the medical literature investigating the use of marijuana in any therapeutic areas. First, we discuss the context for this scientific review. Next, we describe the methods used in this review to identify adequate and well controlled studies evaluating the safety and efficacy of marijuana for particular therapeutic uses.

The FDA conducted a systematic search for published studies in the medical literature that meet the described criteria for study design and outcome measures prior to February 2013. While not part of our systematic review, we have continued to routinely follow the literature beyond that date for subsequent studies. Studies were considered to be relevant to this review if the investigators administered marijuana to patients with a diagnosed medical condition in a well-controlled, double-blind, placebo-controlled clinical trial. Of the eleven studies that met the criteria for review, five different therapeutic areas were investigated:

- Five studies examined chronic neuropathic pain

- Two studies examined appetite stimulation in human immunodeficiency virus (HIV) patients
- Two studies examined glaucoma
- One study examined spasticity and pain in multiple sclerosis (MS)
- One study examined asthma.

For each of these eleven clinical studies, information is provided regarding the subjects studied, the drug conditions tested (including dose and method of administration), other drugs used by subjects during the study, the physiological and subjective measures collected, the outcome of these measures comparing treatment with marijuana to placebo, and the reported and observed adverse events. The conclusions drawn by the investigators are then described, along with potential limitations of these conclusions based on the study design. A brief summary of each study's findings and limitations is provided at the end of the section.

The eleven clinical studies that met the criteria and were evaluated in this review showed positive signals that marijuana may produce a desirable therapeutic outcome, under the specific experimental conditions tested. Notably, it is beyond the scope of this review to determine whether these data demonstrate that marijuana has a currently accepted medical use in the United States. However, this review concludes that these eleven clinical studies serve as proof-of-concept studies, based on the limitations of their study designs, as described in the study summaries. Proof-of-concept studies provide preliminary evidence on a proposed hypothesis regarding a drug's effect. For drugs under development, the effect often

relates to a short-term clinical outcome being investigated. Proof-of-concept studies serve as the link between preclinical studies and dose ranging clinical studies. Therefore, proof-of-concept studies are not sufficient to demonstrate efficacy of a drug because they provide only preliminary information about the effects of a drug. However, the studies reviewed produced positive results, suggesting marijuana should be further evaluated as an adjunct treatment for neuropathic pain, appetite stimulation in HIV patients, and spasticity in MS patients.

The main limitations identified in the eleven studies testing the medical applications of marijuana are listed below:

- The small numbers of subjects enrolled in the studies, which limits the statistical analyses of safety and efficacy.
- The evaluation of marijuana only after acute administration in the studies, which limits the ability to determine efficacy following chronic administration.
- The administration of marijuana typically through smoking, which exposes ill patients to combusted material and introduces problems with determining the doses delivered.
- The potential for subjects to identify whether they received marijuana or placebo, which breaks the blind of the studies.
- The small number of cannabinoid naive subjects, which limits the ability to determine safety and tolerability in these subjects.

- The low number of female subjects, which makes it difficult to generalize the study findings to subjects of both genders.

Thus, this review discusses the following methodological changes that may be made in order to resolve these limitations and improve the design of future studies which examine the safety and efficacy of marijuana for specific therapeutic indications:

- Determine the appropriate number of subjects studied based on recommendations in various FDA Guidances for Industry regarding the conduct of clinical trials for specific medical indications.
- Administer consistent and reproducible doses of marijuana based on recommendations in the FDA Guidance for Industry: Botanical Drug Products (2004).
- Evaluate the effects of marijuana under therapeutic conditions following both acute and chronic administration.
- Consider alternatives to smoked marijuana (*e.g.*, vaporization).
- Address and improve whenever possible the difficulty in blinding of marijuana and placebo treatments in clinical studies.
- Evaluate the effect of prior experience with marijuana with regard to the safety and tolerability of marijuana.
- Strive for gender balance in the subjects used in studies.

In conclusion, the eleven clinical studies conducted to date do not meet the criteria required by the FDA to determine if marijuana is safe and effective in specific therapeutic areas. However, the studies can serve as proof of-concept studies and support further research into the use of marijuana in these therapeutic indications. Additionally, the clinical outcome data and adverse event profiles reported in these published studies can beneficially inform how future research in this area is conducted. Finally, application of the recommendations listed above by investigators when designing future studies could greatly improve the available clinical data that can be used to determine if marijuana has validated and reliable medical applications.

## 1. Introduction

In response to citizen petitions submitted to the Drug Enforcement Administration (DEA) requesting DEA to reschedule marijuana, the DEA Administrator requested that the U.S. Department of Health and Human Services (HHS) provide a scientific and medical evaluation of the available information and a scheduling recommendation for marijuana, in accordance with 21 U.S.C. 811(b). The Secretary of HHS is required to consider in a scientific and medical evaluation eight factors determinative of control under the Controlled Substance Act (CSA). Administrative responsibilities for evaluating a substance for control under the CSA are performed by the Food and Drug Administration (FDA), with the concurrence of the National Institute on Drug Abuse (NIDA). Part of . . .

[ . . . ]

## LETTER FROM U.S. DEPARTMENT OF JUSTICE TO BRYAN KRUMM (JANUARY 16, 2018)

U.S. DEPARTMENT OF JUSTICE
Drug Enforcement Administration
Office of the Administrator
Springfield, VA 22152

Bryan A. Krumm, CNP
733 Monroe, NE
Albuquerque, New Mexico 87110

Dear Mr. Krumm:

This responds to your petition, dated May 22, 2017, asking the Drug Enforcement Administration (DEA) to initiate rule making proceedings pursuant to the Controlled Substances Act (CSA). Specifically you petitioned DEA to propose a rule, pursuant to 21 U.S.C 811(a), to remove marijuana from the CSA schedules. As you know, in August 2016, DEA denied your prior petition to remove marijuana from schedule I.

In response to your prior petition and a separate petition submitted by another group, DEA and the Department of Health and Human Services (HHS) conducted a scientific and medical evaluation and concluded that marijuana must remain in schedule I based on the statutory criteria. According to HHS, marijuana has a high potential for abuse, no currently accepted medical use in treatment in the United States, and a lack of accepted safety for use under medical supervision. As stated in the 2016 Federal Register notices that contained the denials of those petitions (81 FR 53688 and 53767), after considering HHS's scientific and medical evaluation and scheduling

recommendation for marijuana, along with all other relevant data, DEA concluded that there was no substantial evidence to remove marijuana from schedule I.

Your latest petition is based again in large part on your contention that marijuana has a currently accepted medical use in treatment in the United States.[1] However, the information you present in support of that contention fails on its face to meet the established five-part test for demonstrating that a substance has a currently accepted medical use in treatment in the United States. These criteria have been repeatedly set forth by the agency and upheld by the United States Court of Appeals. *See, e.g., Americans for Safe Access v. DEA*, 706 F.3d 438 (D.C. Cir. 2013). As indicated therein, to establish a currently accepted medical use in treatment in the United States for a drug that has not been approved for marketing by the Food and Drug Administration, a petitioner must, among other things, present adequate and well-controlled studies demonstrating the safety and efficacy of that drug. As to this point, your latest petition adds nothing to your prior petition as you

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[1] You also appear to be asking that marijuana be removed entirely from the schedules so that it can be regulated solely by the States, rather than the federal government. Since your desire to remove the federal government from any role in regulating marijuana as a controlled substance-and to transfer such role exclusively to the States-is not a basis for rescheduling under the CSA (and is incompatible with Congress's basic intentions under the Act), it may be rejected without further explanation. You also contend that marijuana does not have a high potential for abuse, yet you provide no support for this contention. Thus, this is merely an empty restatement of a contention that the agency previously rejected in response to your prior petition-which warrants no reevaluation by the agency.

have pointed to no new studies that even purport to establish the safety and efficacy of marijuana. To the contrary, you have simply provided citations to new papers that consist only of reviews of other studies—none of which was designed to, or purports to, demonstrate the safety and efficacy of marijuana. Indeed, the papers to which you cite themselves acknowledge that they are preliminary in nature and would require additional study to draw any definitive conclusions about the safety or efficacy of marijuana.

When Congress enacted the scheduling provisions of the CSA set forth in 21 U.S.C. 811(a) through (c), it did not intend to require the two reviewing agencies (DEA and HHS) to perpetually conduct one eight-factor analysis after another for the same substance every time a prior petition to reschedule that substance was denied—and where a petitioner simply puts forth a cursory claim for rescheduling. While the CSA does require DEA to obtain a scientific and medical evaluation and scheduling recommendation from HHS before initiating proceedings to reschedule a substance, this does not mean DEA must refer every petition to HHS, especially where the petition, on its face, fails to meet the established criteria for rescheduling. It would be an extremely inefficient use of both agencies' resources to conduct such unending analyses based on a submission that plainly fails to materially alter the prior agencies' determination.

For the foregoing reasons, your petition, though accepted for filing, is denied.

Sincerely,

/s/ Robert W. Patterson
Acting Administrator

## LETTER FROM U.S. DEPARTMENT OF JUSTICE TO BRYAN KRUMM (AUGUST 11, 2016)

U.S. DEPARTMENT OF JUSTICE
Drug Enforcement Administration
Office of the Administrator
Springfield, VA 22152

The Honorable Gina M. Raimondo
Governor of Rhode Island
82 Smith Street
Providence, Rhode Island 02903

The Honorable Jay R. Inslee
Governor of Washington
P.O. Box 40002
Olympia, Washington 98504-0002

Mr Bryan A. Krumm

Dear Governor Raimondo, Governor Inslee, and Mr. Krumm:

The enclosed materials provide the legal and factual bases for our decision, in response to your petitions, regarding the rescheduling of marijuana.[1] I will get to that decision, but I will first highlight broader considerations with respect to (1) the law regarding drug scheduling and (2) the current state of marijuana research.

[1] Governors Raimondo and Inslee succeeded Petitioner Governors Chafee and Gregoire, respectively.

**The Law Regarding Drug Scheduling:**

The Controlled Substances Act (CSA) mandates that scheduling decisions be based on medical and scientific data and other data bearing on the relative abuse potential of the drug. Under the CSA, the Food and Drug Administration (FDA), in consultation with the National Institute on Drug Abuse (NIDA), reviews, analyzes, and assesses that data and its medical and scientific conclusions legally bind the Drug Enforcement Administration (DEA).

The FDA and the DEA make a determination based on a full review of the relevant scientific and medical literature regarding marijuana. That process, too, is outlined in the enclosed materials.

A substance is placed in Schedule I if it has no currently accepted medical use in treatment in the United States, a lack of accepted safety for use under medical supervision, and a high potential for abuse. These criteria are set by statute.

Schedule I includes some substances that are exceptionally dangerous and some that are less dangerous (including marijuana, which is less dangerous than some substances in other schedules). That strikes some people as odd, but the criteria for inclusion in Schedule I is not relative danger.

In that sense, drug scheduling is unlike the Saffir-Simpson scale or the Richter scale. Movement up those two scales indicates increasing severity and damage (for hurricanes and earthquakes, respectively); not so with drug scheduling. It is best not to think of drug scheduling as an escalating "danger" scale—rather, specific statutory criteria (based on medical

and scientific evidence) determine into which schedule a substance is placed.

**Marijuana Research:**

Research is the bedrock of science, and we will—as we have for many years—support and promote legitimate research regarding marijuana and its constituent parts. For instance, DEA has never denied an application from a researcher to use lawfully produced marijuana in a study determined by the Department of Health and Human Services (HHS) to be scientifically meritorious.

In fact, during the last two plus years, the total number of individuals and institutions registered with DEA to research marijuana, marijuana extracts, derivatives, and tetrahydrocannabinols (THC) has more than doubled, from 161 in April 2014 to 354 at present. Some of the ongoing research includes studies of the effects of smoked marijuana on human subjects. Folks might be surprised to learn that we support this type of research. But, we do.

DEA and NIDA have also increased the amount of marijuana available for research. Indeed, we consistently meet legitimate demand by researchers for marijuana. Currently. NIDA is filling requests for research marijuana in an average of 25 days.

We will continue to work with NIDA to ensure that there is a sufficient supply of marijuana and its derivatives (in terms of quantity and the variety of chemical constituents) to support legitimate research needs. This includes approving additional growers of marijuana to supply researchers. Details of this pro-

posal to support legitimate research will be published in the Federal Register.

Further, in December 2015, we waived certain regulatory requirements for researchers conducting FDA-authorized clinical trials on cannabidiol (CBD), a constituent part of marijuana. These waivers, when granted, enable researchers to modify or expand the scope of their studies more easily. Currently, there are 90 researchers registered with the DEA to conduct CBD research on human subjects. We have approved every waiver application that has been submitted by these researchers—to date, a total of 47.

If, for instance, CBD proves to be safe and effective for the treatment of a specific medical condition, such as childhood epilepsy (some trials have shown promise), that would be a wonderful and welcome development. But we insist that CBD research—or any research—be sound, scientific, and rigorous before a product can be authorized for medical use. That is specifically—and properly the province of the FDA.

DEA continues to work on other measures to support marijuana research. For instance, DEA is building an online application system for researchers to apply for Schedule I research registrations, including for marijuana. DEA also is drafting clear guidance to assist Schedule I researchers in that application process.

**The Decision:**

The FDA drug approval process for evaluating potential medicines has worked effectively in this country for more than 50 years. It is a thorough, deliberate, and exacting process grounded in science,

and properly so, because the safety of our citizens relies on it.[2]

Using established scientific standards that are consistent with that same FDA drug approval process and based on the FDA's scientific and medical evaluation, as well as the legal standards in the CSA, marijuana will remain a schedule I controlled substance. It does not have a currently accepted medical use in treatment in the United States, there is a lack of accepted safety for its use under medical supervision, and it has a high potential for abuse.

If the scientific understanding about marijuana changes and it could change—then the decision could change. But we will remain tethered to science, as we must, and as the statute demands. It certainly would be odd to rely on science when it suits us and ignore it otherwise.

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[2] The FDA's scientific assessment determines the safety and efficacy of drugs intended for human consumption. The FDA's team, charged with conducting that assessment, consists of clinical pharmacologists, epidemiologists, toxicologists, physicians, chemists, statisticians and other scientists, working together to ensure approved drugs are safe and effective. As our partners at HHS note. "[An] expert [in this discipline) is an individual qualified by scientific training and experience to evaluate the safety and effectiveness of a drug." Although medical doctors are highly trained and qualified to treat patients with FDA-approved drugs, as HHS notes. "[m]edical practitioners who are not experts in evaluating drugs are not qualified to determine whether a drug is generally recognized as safe or effective or meets NDA (New Drug Application) requirements." 57 FR 10499. Simply put, evaluating the safety and effectiveness of drugs for their intended use is a highly specialized endeavor undertaken by the FDA's Center for Drug Evaluation and Research.

The DEA and FDA continue to believe that scientifically valid and well-controlled clinical trials conducted under investigational new drug applications are the proper way to research all potential new medicines, including marijuana. Furthermore, we believe that the drug approval process is the proper way to assess whether a product derived from marijuana or its constituent parts is safe and effective for medical use.

We fully support legitimate medical and scientific research on marijuana and its constituent parts and we will continue to seek ways to make the process for those researchers more efficient and effective.

/s/ Chuck Rosenberg
Acting Administrator

Enclosures

## REPORT: THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS (JANUARY 2017)

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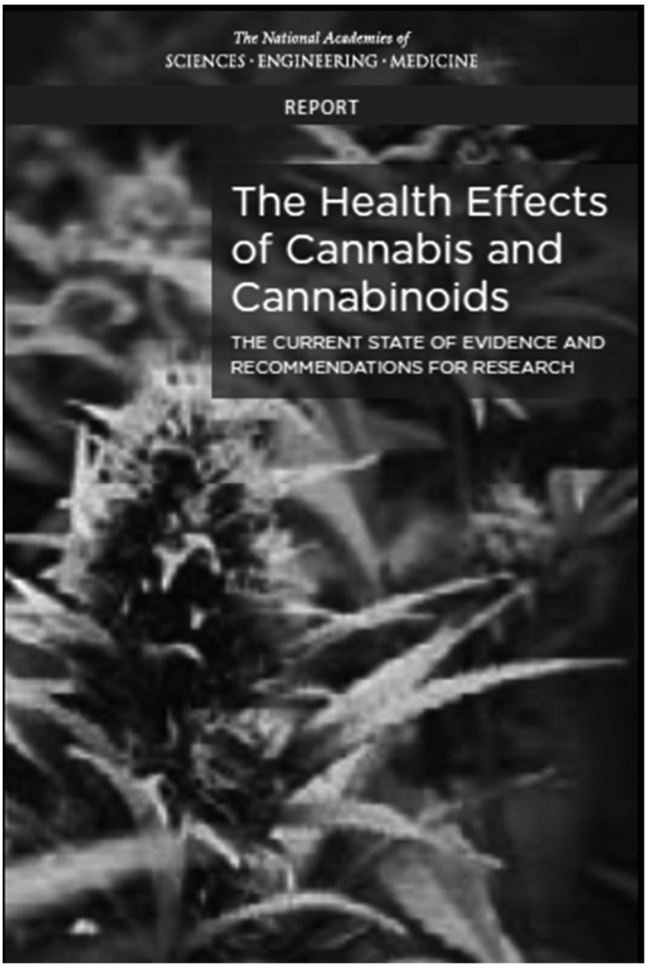
## COMMITTEE'S CONCLUSIONS




In the report THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS: THE CURRENT STATE OF EVIDENCE AND RECOMMENDATIONS FOR RESEARCH, an expert, ad

hoc committee of the National Academies of Sciences, Engineering, and Medicine presents nearly 100 conclusions related to the health effects of cannabis and cannabinoid use.

The committee developed standard language to categorize the weight of the evidence regarding whether cannabis or cannabinoids used for therapeutic purposes are an effective or ineffective treatment for certain prioritized health conditions, or whether cannabis or cannabinoids used primarily for recreational purposes are statistically associated with certain prioritized health conditions. The box on the next page describes these categories and the general parameters for the types of evidence supporting each category.

The numbers in parentheses after each conclusion correspond to chapter conclusion numbers. Each blue header below links to the corresponding chapter in the report, providing much more detail regarding the committee's findings and conclusions. To read the full report, please visit nationalacademies.org/CannabisHealthEffects.

## CONCLUSIONS FOR: THERAPEUTIC EFFECTS

There is conclusive or substantial evidence that cannabis or cannabinoids are effective:

- For the treatment for chronic pain in adults (cannabis) (4-1)
- Antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids) (4-3)

- For improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids) (4-7a)

There is moderate evidence that cannabis or cannabinoids are effective for:

- Improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols) (4-19)

There is limited evidence that cannabis or cannabinoids are effective for:

- Increasing appetite and decreasing weight loss associated with HIV/AIDS (cannabis and oral cannabinoids) (4-4a)
- Improving clinician-measured multiple sclerosis spasticity symptoms (oral cannabinoids) (4-7a)
- Improving symptoms of Tourette syndrome (THC capsules) (4-8)
- Improving anxiety symptoms, as assessed by a public speaking test, in individuals with social anxiety disorders (cannabidiol) (4-17)
- Improving symptoms of posttraumatic stress disorder (nabilone; one single, small fair-quality trial) (4-20)

There is limited evidence of a statistical association between cannabinoids and:

- Better outcomes (*i.e.*, mortality, disability) after a traumatic brain injury or intracranial hemorrhage (4-15)

There is limited evidence that cannabis or cannabinoids are *ineffective* for:

- Improving symptoms associated with dementia (cannabinoids) (4-13)
- Improving intraocular pressure associated with glaucoma (cannabinoids) (4-14)
- Reducing depressive symptoms in individuals with chronic pain or multiple sclerosis (nabiximols, dronabinol, and nabilone) (4-18)

## DEFINITIONS OF WEIGHTS OF EVIDENCE

The committee used the following standardized language to categorize the weight of the evidence regarding cannabis or cannabinoid use for the prioritized health conditions:

### Conclusive Evidence

For therapeutic effects: There is strong evidence from randomized controlled trials to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.

For other health effects: There is strong evidence from randomized controlled trials to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.

For this level of evidence, there are many supportive findings from good-quality studies with no credible opposing findings. A firm conclusion can be

made, and the limitations to the evidence, including chance, bias, and confounding factors, can be ruled out with reasonable confidence.

**Substantial Evidence:**

For therapeutic effects: There is strong evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.

For other health effects: There is strong evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.

For this level of evidence, there are several supportive findings from good-quality studies with very few or no credible opposing findings. A firm conclusion can be made, but minor limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.

**Moderate Evidence:**

For therapeutic effects: There is some evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.

For other health effects: There is some evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.

For this level of evidence, there are several findings from good-to fair-quality studies with very few or no credible opposing findings. A general conclusion can be made, but limitations, including chance, bias,

and confounding factors, cannot be ruled out with reasonable confidence.

**Limited Evidence:**

For therapeutic effects: There is weak evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.

For other health effects: There is weak evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.

For this level of evidence, there are supportive findings from fair-quality studies or mixed findings with most favoring one conclusion. A conclusion can be made, but there is significant uncertainty due to chance, bias, and confounding factors.

**No or Insufficient Evidence to Support the Association:**

For therapeutic effects: There is no or insufficient evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest.

For other health effects: There is no or insufficient evidence to support or refute a statistical association between cannabis or cannabinoid use and the health endpoint of interest.

For this level of evidence, there are mixed findings, a single poor study, or health endpoint has not been studied at all. No conclusion can be made because of substantial uncertainty due to chance, bias, and confounding factors.

There is no or insufficient evidence to support or refute the conclusion that cannabis or cannabinoids are an effective treatment for:

- Cancers, including glioma (cannabinoids) (4-2)
- Cancer-associated anorexia cachexia syndrome and anorexia nervosa (cannabinoids) (4-4b)
- Symptoms of irritable bowel syndrome (dronabinol) (4-5)
- Epilepsy (cannabinoids) (4-6)
- Spasticity in patients with paralysis due to spinal cord injury (cannabinoids) (4-7b)
- Symptoms associated with amyotrophic lateral sclerosis (cannabinoids) (4-9)
- Chorea and certain neuropsychiatric symptoms associated with Huntington's disease (oral cannabinoids) (4-10)
- Motor system symptoms associated with Parkinson's disease or the levodopa-induced dyskinesia (cannabinoids) (4-11)
- Dystonia (nabilone and dronabinol) (4-12)
- Achieving abstinence in the use of addictive substances (cannabinoids) (4-16)
- Mental health outcomes in individuals with schizophrenia or schizophreniform psychosis (cannabidiol) (4-21)
- Conclusions for: Cancer
- There is moderate evidence of no statistical association between cannabis use and:
- Incidence of lung cancer (cannabis smoking) (5-1)
- Incidence of head and neck cancers (5-2)

There is limited evidence of a statistical association between cannabis smoking and:

- Non-seminoma-type testicular germ cell tumors (current, frequent, or chronic cannabis smoking) (5-3)

There is no or insufficient evidence to support or refute a statistical association between cannabis use and:

- Incidence of esophageal cancer (cannabis smoking) (5-4)
- Incidence of prostate cancer, cervical cancer, malignant gliomas, non-Hodgkin lymphoma, penile cancer, anal cancer, Kaposi's sarcoma, or bladder cancer (5-5)
- Subsequent risk of developing acute myeloid leukemia/acute non-lymphoblastic leukemia, acute lymphoblastic leukemia, rhabdomyosarcoma, astrocytoma, or neuroblastoma in offspring (parental cannabis use) (5-6)

## CONCLUSIONS FOR: CARDIOMETABOLIC RISK

There is limited evidence of a statistical association between cannabis use and:

- The triggering of acute myocardial infarction (cannabis smoking) (6-1a)
- Ischemic stroke or subarachnoid hemorrhage (6-2)
- Decreased risk of metabolic syndrome and diabetes (6-3a)
- Increased risk of prediabetes (6-3b)

There is no evidence to support or refute a statistical association between *chronic effects* of cannabis use and:

- The increased risk of acute myocardial infarction (6-1b)

## CONCLUSIONS FOR: RESPIRATORY DISEASE

There is substantial evidence of a statistical association between cannabis smoking and:

- Worse respiratory symptoms and more frequent chronic bronchitis episodes (long-term cannabis smoking) (7-3a)
- There is moderate evidence of a statistical association between cannabis smoking and:
- Improved airway dynamics with acute use, but not with chronic use (7-1a)
- Higher forced vital capacity (FVC) (7-1b)

There is moderate evidence of a statistical association between *the cessation* of cannabis smoking and:

- Improvements in respiratory symptoms (7-3b)

There is limited evidence of a statistical association between cannabis smoking and:

- An increased risk of developing chronic obstructive pulmonary disease (COPD) when controlled for tobacco use (occasional cannabis smoking) (7-2a)

There is no or insufficient evidence to support or refute a statistical association between cannabis smoking and:

- Hospital admissions for COPD (7-2b)

- Asthma development or asthma exacerbation (7-4)

## CONCLUSIONS FOR: IMMUNITY

There is limited evidence of a statistical association between cannabis smoking and:

- A decrease in the production of several inflammatory cytokines in healthy individuals (8-1a)

There is limited evidence of *no* statistical association between cannabis use and:

- The progression of liver fibrosis or hepatic disease in individuals with viral Hepatitis C (HCV) (daily cannabis use) (8-3)

There is no or insufficient evidence to support or refute a statistical association between cannabis use and:

- Other adverse immune cell responses in healthy individuals (cannabis smoking) (8-1b)
- Adverse effects on immune status in individuals with HIV (cannabis or dronabinol use) (8-2)
- Increased incidence of oral human papilloma virus (HPV) (regular cannabis use) (8-4)

## CONCLUSIONS FOR: INJURY AND DEATH

There is substantial evidence of a statistical association between cannabis use and:

- Increased risk of motor vehicle crashes (9-3)

There is moderate evidence of a statistical association between cannabis use and:

- Increased risk of overdose injuries, including respiratory distress, among pediatric populations in U.S. states where cannabis is legal (9-4b)

There is no or insufficient evidence to support or refute a statistical association between cannabis use and:

- All-cause mortality (self-reported cannabis use) (9-1)
- Occupational accidents or injuries (general, non-medical cannabis use) (9-2)
- Death due to cannabis overdose (9-4a)

## CONCLUSIONS FOR: PRENATAL, PERINATAL, AND NEONATAL EXPOSURE

There is substantial evidence of a statistical association between maternal cannabis smoking and:

- Lower birth weight of the offspring (10-2)
- There is limited evidence of a statistical association between maternal cannabis smoking and:
- Pregnancy complications for the mother (10-1)
- Admission of the infant to the neonatal intensive care unit (NICU) (10-3)

There is insufficient evidence to support or refute a statistical association between maternal cannabis smoking and:

- Later outcomes in the offspring (*e.g.*, sudden infant death syndrome, cognition/academic achievement, and later substance use) (10-4)

## CONCLUSIONS FOR: PSYCHOSOCIAL

There is moderate evidence of a statistical association between cannabis use and:

- The impairment in the cognitive domains of learning, memory, and attention (acute cannabis use) (11-1a)

There is limited evidence of a statistical association between cannabis use and:

- Impaired academic achievement and education outcomes (11-2)
- Increased rates of unemployment and/or low income (11-3)
- Impaired social functioning or engagement in developmentally appropriate social roles (11-4)

There is limited evidence of a statistical association between *sustained abstinence from* cannabis use and:

- Impairments in the cognitive domains of learning, memory, and attention (11-1b)

## CONCLUSIONS FOR: MENTAL HEALTH

There is substantial evidence of a statistical association between cannabis use and:

- The development of schizophrenia or other psychoses, with the highest risk among the most frequent users (12-1)

There is moderate evidence of a statistical association between cannabis use and:

- Better cognitive performance among individuals with psychotic disorders and a history of cannabis use (12-2a)
- Increased symptoms of mania and hypomania in individuals diagnosed with bipolar disorders (regular cannabis use) (12-4)
- A small increased risk for the development of depressive disorders (12-5)
- Increased incidence of suicidal ideation and suicide attempts with a higher incidence among heavier users (12-7a)
- Increased incidence of suicide completion (12-7b)
- Increased incidence of social anxiety disorder (regular cannabis use) (12-8b)

There is moderate evidence of no statistical association between cannabis use and:

- Worsening of negative symptoms of schizophrenia (*e.g.*, blunted affect) among individuals with psychotic disorders (12-2c)

There is limited evidence of a statistical association between cannabis use and:

- An increase in positive symptoms of schizophrenia (*e.g.*, hallucinations) among individuals with psychotic disorders (12-2b)
- The likelihood of developing bipolar disorder, particularly among regular or daily users (12-3)
- The development of any type of anxiety disorder, except social anxiety disorder (12-8a)
- Increased symptoms of anxiety (near daily cannabis use) (12-9)

- Increased severity of posttraumatic stress disorder symptoms among individuals with posttraumatic stress disorder (12-11)

There is no evidence to support or refute a statistical association between cannabis use and:

- Changes in the course or symptoms of depressive disorders (12-6)
- The development of posttraumatic stress Disorder (12-10)

## CONCLUSIONS FOR: PROBLEM CANNABIS USE

There is substantial evidence that:

- Stimulant treatment of attention deficit hyperactivity disorder (ADHD) during adolescence is *not* a risk factor for the development of problem cannabis use (13-2e)
- Being male and smoking cigarettes are risk factors for the progression of cannabis use to problem cannabis use (13-2i)
- Initiating cannabis use at an earlier age is a risk factor for the development of problem cannabis use (13-2j)

There is substantial evidence of a statistical association between:

- Increases in cannabis use frequency and the progression to developing problem cannabis use (13-1)
- Being male and the severity of problem cannabis use, but the recurrence of problem cannabis use does not differ between males and females (13-3b)

There is moderate evidence that:

- Anxiety, personality disorders, and bipolar disorders are *not* risk factors for the development of problem cannabis use (13-2b)
- Major depressive disorder is a risk factor for the development of problem cannabis use (13-2c)
- Adolescent ADHD is *not* a risk factor for the development of problem cannabis use (13-2d)
- Being male is a risk factor for the development of problem cannabis use (13-2f)
- Exposure to the combined use of abused drugs is a risk factor for the development of problem cannabis use (13-2g)
- Neither alcohol nor nicotine dependence alone are risk factors for the progression from cannabis use to problem cannabis use (13-2h)
- During adolescence the frequency of cannabis use, oppositional behaviors, a younger age of first alcohol use, nicotine use, parental substance use, poor school performance, antisocial behaviors, and childhood sexual abuse are risk factors for the development of problem cannabis use (13-2k)

There is moderate evidence of a statistical association between:

- A persistence of problem cannabis use and a history of psychiatric treatment (13-3a)
- Problem cannabis use and increased severity of posttraumatic stress disorder symptoms (13-3c)

There is limited evidence that:

- Childhood anxiety and childhood depression are risk factors for the development of problem cannabis use (13-2a)

## CONCLUSIONS FOR: ABUSE OF OTHER SUBSTANCES

There is moderate evidence of a statistical association between cannabis use and:

- The development of substance dependence and/or substance abuse disorder for substances including alcohol, tobacco, and other illicit drugs (14-3)

There is limited evidence of a statistical association between cannabis use and:

- The initiation of tobacco use (14-1)
- Changes in the rates and use patterns of other licit and illicit substances (14-2)

## CONCLUSIONS FOR: CHALLENGES AND BARRIERS IN CONDUCTING CANNABIS AND CANNABINOID RESEARCH

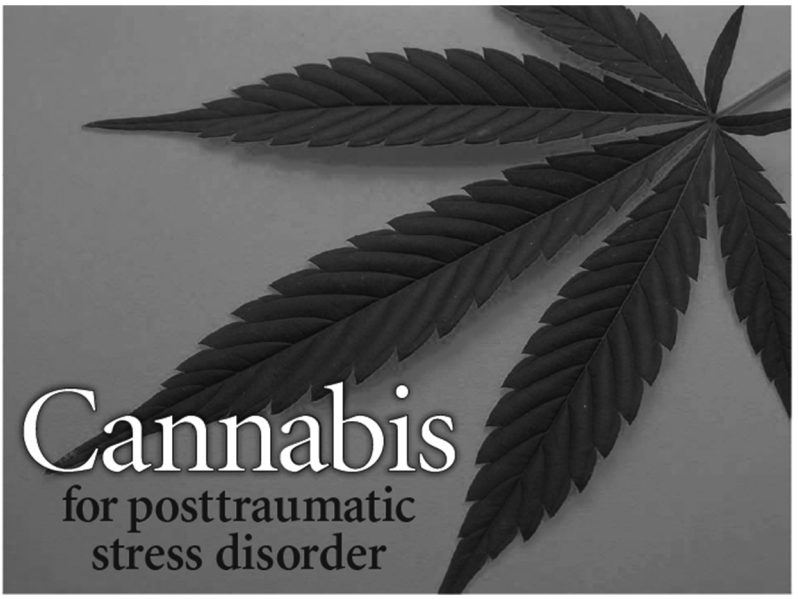
There are several challenges and barriers in conducting cannabis and cannabinoid research, including:

- There are specific regulatory barriers, including the classification of cannabis as a Schedule I substance, that impede the advancement of cannabis and cannabinoid research (15-1)
- It is often difficult for researchers to gain access to the quantity, quality, and type of cannabis product necessary to address specific research

questions on the health effects of cannabis use (15-2)

- A diverse network of funders is needed to support cannabis and cannabinoid research that explores the beneficial and harmful effects of cannabis use (15-3)
- To develop conclusive evidence for the effects of cannabis use for short-and long-term health outcomes, improvements and standardization in research methodology (including those used in controlled trials and observational studies) are needed (15-4)

# REPORT: CANNABIS FOR POSTTRAUMATIC STRESS DISORDER




## A neurobiological approach to treatment

*Abstract: The endocannabinoid system is intricately involved in regulation of the neurobiological processes, which underlie the symptomatology of posttraumatic stress disorder (PTSD). This article discusses the neurobiological underpinnings of PTSD and the use of cannabis for treating PTSD in the New Mexico Medical Cannabis Program.*

**By Bryan A. Krumm, MSN, RN, CNP, BC**

The State of New Mexico has approved post-traumatic stress disorder (PTSD) as an indication for its Medical Cannabis Program, and patients with PTSD currently comprise the largest segment of any approved indication.

Cannabis remains in Schedule I of the Controlled Substances Act (CSA) in the United States, making it illegal to use under federal law. In the case of Krumm vs. Holder, the Drug Enforcement Administration argued that they did not need to defer to state laws regarding scheduling decisions for controlled substances. Due to the federal prohibition against cannabis, research looking into its therapeutic value has faced significant barriers, rendering it nearly impossible to conduct controlled clinical trials of cannabis in treating PTSD. However, the U.S. Supreme Court has upheld that practitioners have a right to recommend cannabis to patients when it is deemed appropriate.

PTSD can occur when a patient is exposed to one or more traumatic events leading to the development of characteristic symptoms following exposure. Patients may exhibit fear-based re-experiencing with emotional and behavioral symptoms. Others may present with an-hedonic or dysphoric states and negative cognition. Patients may exhibit arousal and reactive-externalizing, while others may exhibit dissociative symptoms. Some individuals may have combinations of symptom patterns. PTSD is considered the fourth most common psychiatric disorder, affecting 10% of all men and 18% of women, with rates approximately 40% in high-trauma populations, such as soldiers in combat, low-income individuals, and those living in inner cities. PTSD often occurs comorbidly with other psychiatric disorders. Originally, PTSD was considered a normative response, related primarily to stressor intensity, but individual response to trauma depends on stressor characteristics as well as neurobiological factors.

The endocannabinoid system appears to be involved in the extinction of aversive memories, and patients with PTSD claim that cannabis use helps alleviate their symptoms. Cannabinoids stimulate receptors in the prefrontal cortex, amygdala, and hippocampus, activating signaling pathways, which appear to inhibit anxiety.' Alterations in the endocannabinoid system are seen in depression, including changes in levels of cannabinoid 1 (CB1) receptors and endogenous CB1 receptor ligands. Stimulation of cannabinoid receptors enhances stress-coping behaviors and increases spontaneous firing of serotonergic and noradrenergic neurons in the midbrain. Phytocannabinoids, including delta 9 tetrahydrocannabinol (THC), cannabidiol (CBD), and cannabichromene exert antidepressant-like actions and may be useful in the treatment of mood disorders.

High rates of suicidal behavior have been found among patients with PTSD. It appears that sensitization of CB1receptormediated G-protein signaling in the prefrontal cortex contributes to the pathophysiology of suicide and likely contributes to suicidal behavior. The role of the endocannabinoid system in the pathophysiology of PTSD suggests that cannabinoids may be an effective modality to treat both PTSD and suicidal behavior in patients with PTSD. Many patients in New Mexico's Medical Cannabis Program for PTSD have reported reductions in frequency and severity of suicidal thoughts at Medical Advisory Board meetings. Some reported complete cessation of suicidality.

The military is currently facing an epidemic of suicide, and the U.S. Department of Veterans Affairs has called on all mental health and substance abuse

healthcare providers to share responsibility for zero tolerance regarding suicide. An estimated 22 veterans die via suicide daily, accounting for at least 22.2% of all reported suicides. There were also 349 suicides among active duty troops in 2012, accounting for more deaths than by enemy fire. Developing new treatment modalities for PTSD is critical given the number of returning veterans who require psychiatric help and are at high risk for suicide.

Raphael Mechoulam, PhD, perhaps the world's leading authority on cannabinoids and the endo-cannabinoid system, points out the following:

> "It has been suggested that pharmacologic treatments in psychiatry have been overly reliant on neurotransmitter systems and their agonists. In the last several decades, advances in psychopharmacology have reduced adverse reactions but have failed to lead to major disease improvement. The endocannabinoid system may shed new light on the physiologic basis of psychiatric diseases, leading to new and more effective treatments."

## The Neurobiological Basis of PTSD

After exposure to a traumatic event, patients may experience recurring memories of the event, including distressing dreams, dissociative reactions/ flashbacks, or increased stress responses to external cues and physiological reactions to external cues resembling aspects of the traumatic event. They try to avoid distressing memories or external reminders of the event. They experience negative changes in mood and cognition associated with the event in addition to

marked alterations in arousal and reactivity, beginning or worsening after the traumatic event. These disturbances continue for over 1 month and cause significant disturbances in social, occupational, or other important areas of function. These disturbances cannot be attributable to the physiological effects of substances or other medical conditions.

The broad range of symptoms seen in PTSD have made treatment challenging. PTSD involves central neurotransmitter imbalances and neuroanatomical disruptions, with potential dysregulation of immune, autonomic, endocrine, and cardiovascular function. Recent neuroimaging studies have helped elucidate the underlying neurobiological processes involved in the symptomatology of PTSD as well as the role of the endocannabinoid system in managing these neurobiological pathways. CB1 receptor availability is upregulated in an amygdala-hippocampal-cortico-striatal neural circuit implicated in PTSD and in brain regions outside this circuit. This may result from a combination of both receptor upregulation and low receptor occupancy by anandamide, an endogenous cannabioid. This suggests that abnormal CB1 receptor-mediated anandamide signaling is implicated in the PTSD etiology.

PTSD is associated with amygdala dysfunction, the anterior cingulate cortex (ACC), the medial prefrontal cortex (mPFC), and the hippocampus. Structural impairments include decreased hippocampal volume and decreased ACC volume. Dysregulation in threat-related processing in response to trauma exposure leads to a cascade of neural changes, causing a state of amygdala hyper-responsivity, which triggers hyperarousal and vigilance. Inadequate topdown control

by the mPFC and ACC perpetuates the state of amygdala hyperresponsivity, increasing attention to trauma-related stimuli.

The hypothalamic-pituitary-adrenal (HPA) axis coordinates neuroendocrine stress response systems and has been a major focus of scrutiny in patients with PTSD. Exposure to stress triggers neurons in the hypothalamic paraventricular nucleus to secrete a corticotropin-releasing hormone, which stimulates the production and release of adrenocorticotropic hormone (ACTH) from the anterior pituitary. ACTH then stimulates the release of glucocorticoids from the adrenal cortex, which modulate metabolism, immune function, and brain function to manage stressors. Sustained glucocorticoid exposure leads to reduced dendritic branching, loss of dendritic spines, and impaired neurogenesis of the hippocampus.

## Role of the Endocannabinoid System in PTSD

THC has a significant and selective impact on amygdala reactivity to threat signals in humans. Endocannabinoids are crucial for the extinction of aversive memories. Activation of CB1 receptors in the amygdala blocks reconsolidation of aversive memories, which suggests that cannabinoids might help patients with PTSD prevent relapse after a stressful experience.

The endocannabinoid system plays a significant role in the function of the prefrontal cortex. The PFC receives and modulates information processing throughout the brain and projects to subcortical arousal systems, regulating monoamine and cholinergic inputs. Activation of cannabinoid receptors in the mPFC enhances serotonin 5hydroxytryptamine (5HT) neurotransmission, eliciting potent antidepressant effects.

Disinhibition of excitatory projections from the mPFC to serotonergic neurons in the dorsal raphe may underlie antidepressant activity in the mPFC. The endocannabinoid system may be involved not only in the extinction of conditioned fear but also adaptation to aversive situations in general.

Cannabinoids have diverse effects on hippocampal memory and plasticity. The effects of cannabinoids on anxiety appear to be biphasic, with low doses being anxiolytic and high doses being ineffective or possibly anxiogenic. However, chronic high-dose cannabinoid treatment has been shown to induce hippocampal neurogenesis, which may contribute to the anxiolytic and antidepressant effects of cannabinoids. Modulation of hippocampal memory and plasticity by targeting the endocannabinoid system may aid in the treatment of impaired extinction-like processes seen in PTSD.

Endocannabinoid signaling negatively modulates function of the HPA axis. Short-term activation of the HPA axis is beneficial to survival; however, long-term activation can impact mood, cognition, and metabolism. Chronic activation of the HPA axis is associated with a variety of neuropsychiatric disorders.

Cannabinoids, through action on both limbic and paralimbic brain areas, reduce activity of the amygdala and hypothalamus. Retrograde endocannabinoid signaling in the hypothalamus is responsible for regulating HPA output. Acute administration of exogenous cannabinoid ligands also activates the HPA axis indirectly through an increase in serotonergic and noradrenergic neurotransmission. Chronic exposure to desipramine (and perhaps other antidepressants and therapies) has been shown to upregulate the endocannabinoid

system, which, in turn, dampens the stress axis in a manner similar to habituation. Endogenous cannabinoid signaling is essential for stress adaptation and is fundamental to the intrinsic regulation of the HPA axis.

## Discussion

Because PTSD is often difficult to treat with a single medication, it is common to see the use of "drug cocktails," which may cause significant adverse reactions. This may include treatment with combinations of antidepressants, antipsychotics, benzodiazepines, anticonvulsants, sedative/hypnotics, and antihypertensives. Cannabis may address symptoms across all 3 major symptom clusters in PTSD with few clinically significant adverse reactions.

A review by Grant and colleagues found that inhaled cannabis is a rapid and efficient method of delivery for THC, allowing for self-titration of medication. Although cannabis may cause dizziness, anxiety, paranoia, dry mouth, fatigue, or weakness, tolerance to adverse reactions develops rapidly. There are no reports of fatal overdose with cannabis, and long-term use is not associated with increased risk of lung or gastrointestinal cancers. There is little evidence of important CYP 450 system drug-drug interactions, and the acute medical risks of THC as used in clinical trials are low.

Inhaled cannabis is generally well tolerated and has been shown to reduce the pain intensity, decrease anxiety, and improve sleep. Cannabinoids may reduce or entirely eliminate nightmares; patients using cannabinoids report improvement in sleep time, quality of

sleep, and reduction of daytime flashbacks and night sweats.

Alcohol abuse has been significantly linked to PTSD, and cannabis has been shown to act as a substitute for alcohol. Many patients with PTSD struggle with alcohol abuse, often in an attempt to self-medicate. The majority of these patients referred to the Medical Cannabis Program, who have co-occurring alcohol abuse issues, have reported significantly decreased use, and in many cases, complete cessation of alcohol. A patient survey conducted by Berkeley Patient's Group, a medical cannabis dispensary in Berkeley, CA, found that 65% of those surveyed reported using cannabis as a substitute because it has less adverse reactions than alcohol and illicit or prescription drugs.

Cannabinoids have been shown to reduce aggressive behavior, which has important implications in PTSD. Patients commonly report significant reductions in irritability and anger. Patients are often accompanied by family members, friends, and/or treatment team members who confirm reductions in aggressive behavior.

Many patients with PTSD have co-occurring psychotic disorders. Although use of cannabis in patients with schizophrenia has typically been reported to worsen psychosis, increases in population cannabis use have not been followed by increases in psychotic incidence. THC has been shown to improve symptoms in treatment-refractory patients with schizophrenia, including reduction in core psychotic symptoms, with no clinically significant adverse effects. When compared to non-using patients, patients with schizophrenia who use cannabis and patients with a history of canna-

bis at first episode of psychosis have superior neuropsychological functioning. Medical cannabis patients with co-occurring psychotic disorders often report reductions in both positive and negative symptoms of schizophrenia, which have failed to resolve with traditional antipsychotic medications, consistent with the findings of Schwarcz and colleagues.

Strains of cannabis-containing CBD in addition to THC may prevent the psychotic-like symptoms sometimes caused by strains with high levels of THC but a lack of CBD. Cannabis of the *sativa* and *ruderalis* biotypes typically contain higher levels of CBD and lower levels of THC, while *indica* biotypes tend to have higher levels of THC and more variable levels of CBD. Unfortunately, finding consistent access to CBDrich strains is difficult for many patients, and finding the best strain for any individual is largely a matter of trial and error.

***PTSD is considered the fourth most common psychiatric disorder, affecting 10% of all men and 18% of women.***

A comprehensive study of 4 legal, medical cannabis patients in the federal Investigational New Drug Program found only mild changes in pulmonary function associated with long-term, heavy use. No functionally significant adverse effects were noted in any other physiologic system examined in the study. Although changes in pulmonary function can be seen with chronic high use of cannabis, occasional and low cumulative marijuana use of up to 1 joint a day for 7

years is not associated with adverse effects on pulmonary function.

New Mexico incorporated a definition of "practitioner" that allows advanced practice nurses with prescriptive authority to refer patients to the Medical Cannabis Program. Unfortunately, most states with medical cannabis programs do not allow advanced practice nurses to refer patients. Many providers are not able to refer patients to medical cannabis programs due to institutional regulations. Some providers may have concerns about potential adverse reactions reported with cannabis. However, for those who are able and willing to refer patients to medical cannabis programs, these programs offer a unique opportunity to investigate the safety and efficacy of cannabis while providing relief from pain and suffering.

## Marijuana as Medicine

Cannabis is effective in treating PTSD, even when there are other co-occurring psychiatric and/or medical disorders. The broad range of therapeutic effects seen in treating PTSD with cannabis suggests that it may be beneficial in treating other disorders as well. Rather than targeting neurotransmitter systems and their agonists, cannabinoids target the underlying neurobiological processes that lead to imbalances in these neurotransmitter systems, helping to return them to a state of homeostasis.

As with any medication, caution must be used when recommending medical cannabis. Patients should be warned of potential risks, including the potential legal and occupational repercussions that can arise the use of cannabis. Some patients may experience increased levels of sedation, anxiety, or paranoia,

and cannabis may induce psychosis in certain individuals. Many patients may opt to use cannabis in spite of these risks.

"Based on evidence currently available, the Schedule I classification is not tenable; it is not accurate that cannabis has no medical value or that information on safety is lacking." Healthcare providers have an obligation to provide the best possible care based on the best available scientific evidence. Until cannabis is removed from Schedule I of the federal CSA, the barriers to controlled clinical trials of cannabis in treating PTSD and other medical conditions will remain.