

In the United States Court of Appeals
for the Ninth Circuit

SUZANNE SISLEY, M.D.; SCOTTSDALE RESEARCH INSTITUTE, LLC; BATTLEFIELD
FOUNDATION, DBA FIELD TO HEALED; LORENZO SULLIVAN; KENDRICK SPEAGLE;
GARY HESS,

Petitioners,

v.

U.S. DRUG ENFORCEMENT ADMINISTRATION; WILLIAM BARR, ATTORNEY GENERAL;
TIMOTHY SHEA, ACTING ADMINISTRATOR, DRUG ENFORCEMENT ADMINISTRATION,

Respondents

**AMICUS CURIAE BRIEF OF RICE UNIVERSITY'S BAKER INSTITUTE
OF PUBLIC POLICY, DRUG POLICY PROGRAM, DR. KEVIN
BOEHNKE AND DR. DANIEL CLAUW
IN SUPPORT OF PETITIONERS' PETITION FOR REVIEW**

Lisa L. Pittman
COATS ROSE, P.C.
Terrace Two
2700 Via Fortuna, Suite 350
Austin, Texas 78746-7911
Telephone 512.469.7987
Facsimile 512.469.9408
lpittman@coatsrose.com

ATTORNEY FOR AMICI RICE UNIVERSITY'S
BAKER INSTITUTE OF PUBLIC POLICY, DRUG
POLICY PROGRAM; DR. KEVIN BOEHNKE;
DR. DANIEL CLAUW

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CORPORATE DISCLOSURE STATEMENT

Amicus Baker Institute for Public Policy, Drug Policy Program, is a non-profit research and policy institute affiliated with Rice University in Houston, Texas. The Institute does not have any parent companies, subsidiaries, or affiliates that have issued shares to the public. Amici Drs. Kevin Boehnke and Dan Clauw are research scientists.

All Parties have consented to the filing of this amicus brief. No counsel for any party authored the brief in whole or in part, nor did any person or entity other than Amici Curiae or their counsel make any monetary contribution to the preparation or submission of this Brief.

INTEREST OF AMICI CURIAE:

Founded in 1993, Rice University's Baker Institute for Public Policy (the "Institute") is one of the country's premier nonpartisan public policy think tanks. Named for former Secretary of State James Baker, the Institute is guided by his vision that practical imperatives must impact public policy. An integral part of Rice University, one of the nation's most distinguished and high-ranking universities, the Institute's achievements are supported by its fellows, scholars, Rice faculty, and staff.

Begun in 2001, the Baker Institute Drug Policy Program ("Program") pursues research and debate on drug policies to develop pragmatic solutions based on common sense and human rights interests to focus on reducing death, disease, crime and suffering associated with drug use, legal and illegal. The Program has hosted then-

current DEA Administrator Asa Hutchinson, then-current National Drug Policy Director John Walters, former Director Lee Brown, and Kevin Sabet, co-founder of Smart Approaches to Marijuana.

William Martin, Ph.D., and Katharine Neill Harris, Ph.D., resident Program Directors/Fellows, have researched, written, lectured, lobbied, and testified on reduction/removal of criminal penalties for low-level nonviolent drug use, marijuana regulation and taxation, and marijuana therapeutics. After interviewing many veterans who have successfully managed their PTSD with marijuana, Drs. Martin and Harris were led to Dr. Suzanne Sisley's work. The Program follows her efforts to perform critically needed scientific research about the potential benefits of marijuana for treating PTSD. The Program shares her frustration over the difficulties she has faced because of obstacles that hinder research that might challenge the assumption that marijuana belongs in Schedule I.

The Program is aware of the complexities involved in scientific research on marijuana. This amicus brief is filed because the solution is not to prohibit all research; but rather to facilitate and encourage research, using a variety of marijuana products from numerous vetted producers, with a variety of research participants, in particular, afflicted veterans and those suffering from opioid dependency and abuse.

Dr. Kevin Boehnke is a Research Investigator at the University of Michigan, Ann Arbor. He studies chronic pain and cannabis, with a special emphasis on the

intersection of cannabis and opioids. Dr. Daniel Clauw is a Professor of Anesthesiology, Medicine (Rheumatology) and Psychiatry at the University of Michigan, Ann Arbor, where he serves as Director of the Chronic Pain and Fatigue Research Center. Dr. Clauw is a recognized thought-leader in chronic pain research, known for his pioneering contributions to evidence-based understanding of chronic pain mechanisms and chronic pain management. Drs. Boehnke and Clauw helped develop the Arthritis Foundation's first and only guidance documents on CBD and have offered expert guidance on how best to use cannabis for chronic pain management, as reported in the 2019 *Annals of Internal Medicine*. Drs. Boehnke and Clauw support this amicus brief as proponents for allowing uncompromised cannabis research to better develop the pharmacopeia and to discover what forms of cannabis treatments may help certain populations dealing with pain and opioid abuse.

Amici submit this brief in support of Dr. Sisley, the Scottsdale Research Institute, and the other Petitioners to elucidate the public policy imperatives, backed by scientific data, which support Petitioners' legal arguments. Amici encourage this Court to grant Petitioners' petition, find that the DEA's conclusion that marijuana has no accepted medical use is arbitrary, capricious, and contrary to the medical conclusions in a supermajority of the States, and to require a reconsideration of scheduling and facilitation of research.

SUMMARY OF ARGUMENT

The fact that someone can legally, but unscientifically, self-medicate with marijuana unsupervised in one building, but cannot have a physician administer a scientific dose in a monitored study in the building next door, is an untenable situation that ignores current reality and robs us of scientific discoveries and potential treatment options. The DEA's continued inaction and refusal to allow real world research on marijuana, despite 47 states' determination that marijuana has some medical potential, stifles the development of the very research that, if recognized, would justify the removal of marijuana from Schedule I, and thus beget more research. Forbidding research continues to harm all those who could benefit from it.

The public policy arguments made here detail scientific studies performed to date about marijuana's effectiveness for treating pain and reducing opioid misuse, which could also benefit those suffering from post-traumatic stress disorder ("PTSD"), who are often prescribed a panoply of medications. Dr. Sisley specifically endeavors to research the healing interaction between marijuana and PTSD to treat U.S. veterans in a scientifically measured way.

In 1970, President Richard Nixon signed into law the Controlled Substances Act ("CSA"), which placed marijuana on Schedule I. Despite the flexibility intended by the scheduling regime, and despite fifty years of petitions, there it inexplicably remains. It is time to reconsider the blind dogmatic adherence to this position, as the States and

other countries have already done. The World Health Organization has already descheduled low THC cannabis (hemp CBD) and is scheduled to reconsider marijuana this year—it has been conducting hearings of evidence in furtherance its removal from the 1961 Single Convention on Narcotic Drugs. It is time the United States consider current medical uses for marijuana as well and revisit the original scheduling determination, applying currently medically acceptable treatments with it. To date the Drug Enforcement Administration (“DEA”) has employed a results oriented approach to marijuana scheduling, ignoring currently accepted medical treatment. This brief is submitted in support of the premise that medical science should prevail.

Amici urge this Court to grant Petitioners’ petition for review, and to find that DEA’s retention of marijuana on Schedule I of the Controlled Substances Act is arbitrary and capricious, given current medically accepted uses throughout the States and the world.

ARGUMENT

I. **As a Practical Imperative, Marijuana Research Is Necessary to Follow Mass Statewide Legalization**

A. **Research Obstructed and Impeded**

Marijuana’s Schedule I status prevents research and development of marijuana-derived pharmaceuticals. Schedule I controlled substances are defined as substances with high potential for abuse and no currently accepted safe medical use, even when supervised by a physician, resulting in unduly onerous regulatory hurdles for any attempted research.¹ As more state-legal marijuana markets emerge, and as marijuana² products diversify, government officials should not ignore commercialization, but instead, study it to create policies based on best practices for public health and protection.³

To research Schedule I controlled substances, scientists must obtain difficult and time-consuming approvals from DEA. Further, state-legal marijuana program licensees

¹ 21 USC § 812(b)(1).

² United States Commission on Marihuana and Drug Abuse, *Marihuana: A Signal of Misunderstanding: First Report*, 184 (1972); RC Randall, United States Drug Enforcement Administration, *Marijuana, Medicine & the Law* (Vol. 1 1988).

³ C.M. Bowling, A.Y. Hafez, S.A. Glantz, *Public Health and Medicine’s Need to Respond to Marijuana Commercialization in the United States: A Commentary*, JOURNAL OF PSYCHOACTIVE DRUGS, 1–6 (2020); J. Marcu, *Regulators Need to Rethink Restrictions on Marijuana Research*, NATURE, 572, S19–S19 (2019); Russo EB, Mead AP, Sulak D., *Current Status and Future of Marijuana Research*, CLINICAL RESEARCHER, 58-63 (April 2015); A. Mead, *The Legal Status of Marijuana (Marijuana) and Cannabidiol (CBD) Under U.S. Law*, EPILEPSY & BEHAVIOR, 70, 288-91, (May 2017).

cannot obtain DEA approval because the application disqualifies anyone already growing marijuana, despite the expertise that experience and those products would lend to research.

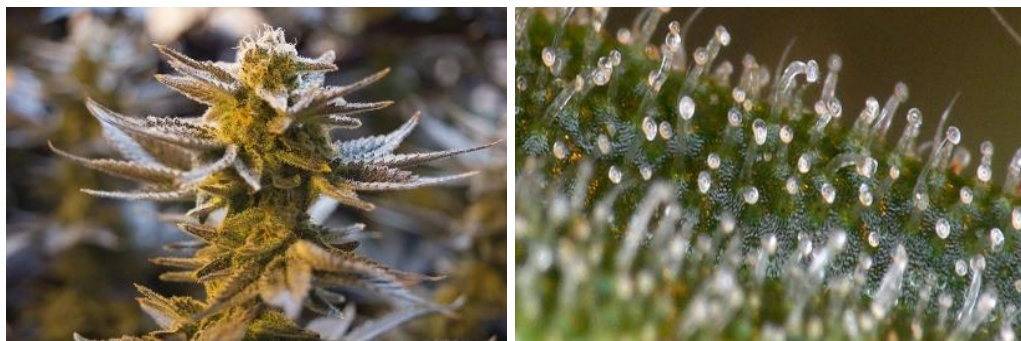
As recounted in Petitioners' brief, researchers are limited to NIDA University of Mississippi marijuana, which does not mirror products available to actual consumers. This sole-source prevents researchers from studying the effect of a plant's full cannabinoid expression as contained in the trichomes of the outer leaves, which are crushed and eviscerated by the NIDA marijuana.⁴ The NIDA pulverization shaves off the valuable trichomes, but in commercial marijuana, they are preserved through proper trimming, curing, and drying.⁵ Moreover, NIDA marijuana contains less than 50% of the cannabinoid concentration than state-legal marijuana and often 80% fewer terpenes, another therapeutic cannabinoid component of marijuana lost by long periods of storage as it becomes embrittled.⁶

⁴ <https://coloradamarijuanatours.com/guides/trichomes-terpenes-types-uses/>.

⁵ <https://www.leafly.com/news/cannabis-101/what-are-trichomes-on-cannabis#:~:text=The%20actual%20definition%20of%20trichome,of%20a%20science%20fiction%20novel.>

⁶ EB Russo, ML Mathre, A Byrne, R Velin, PJ Bach, J Sanchez-Ramos, *et al.*, *Chronic Marijuana Use in the Compassionate Investigational New Drug Program: an Examination of the Benefits and Adverse Effects of Legal Clinical Marijuana*, JOURNAL OF MARIJUANA THERAPEUTICS, 2:1, 3-57 (2002); RN Bloor, TS Wang, P Spanel, D Smith, *Ammonia Release from Heated 'Street' Marijuana Leaf and Its Potential Toxic Effects on Marijuana Users*, ADDICTION, 103 (2008); EB Russo, *Current Therapeutic Marijuana Controversies and Clinical Trial Design Issues*, FRONT PHARMACOL, 7:309 (2016); <https://coloradamarijuanatours.com/guides/trichomes-terpenes-types-uses/>.

Here are pictures of commercially available fresh leafy marijuana, the first displaying fully expressed trichomes, and the second showing the delicate trichomes under a microscope:



In addition to Petitioners’ arguments, Amici posit the Schedule I status has created obstacles that have been detrimental to America’s public health. The federal scheduling of marijuana is of significant public concern because the Schedule I status prevents researchers from conducting appropriate research to gather medical and scientific data, and its federal prohibition constitutes an overreach into a healthcare matter which should be one of local control. As such, many states deemed medical marijuana businesses “essential” during the COVID pandemic.

B. Incongruent Federal Position

At the same time the DEA is maintaining marijuana at Schedule I status and denying research, incongruently, DEA is not allowed by Congress to enforce the CSA directly against state-compliant medical marijuana businesses. In 2009, the Department of Justice (“DOJ”) issued a memorandum directed at U.S. attorneys indicating that the

federal government would not devote its resources to prosecuting “individuals whose actions are in clear and unambiguous compliance with existing state laws providing for the medical use of marijuana.”⁷ Since 2014, Congress has expressly prohibited the DEA and DOJ from using appropriated funds to block states from implementing laws that authorize the use, distribution, possession, or cultivation of medical marijuana. (“Funding Riders,” also referred to as the “Joyce-Blumenauer Amendment”).⁸ The Funding Riders were enacted after the DOJ’s 2013 “Cole Memorandum” prosecutorial enforcement priority direction from then Attorney General James Cole that recognized state legalization of marijuana.

Despite a change in administration, the Department still does not prioritize enforcement of the CSA for individuals using medical marijuana under state law. *See Confirmation Hearing on the Nomination of Hon. William Pelham Barr to be Attorney General of the United States: Hearing Before the S. Judiciary Comm.*, S. Hrg. 116-65, 116th Cong., at 70 (2019) (statement of William P. Barr) (“My approach to this would be not to upset

⁷ Mem. from David W. Ogden, Deputy Att’y Gen., U.S. Dep’t of Justice, to Selected U.S. Att’ys, 1-2 (Oct. 19, 2009), available at <https://www.justice.gov/sites/default/files/opa/legacy/2009/10/19/medical-marijuana.pdf>.

⁸ C.M. Bowling, A.Y. Hafez, S.A. Glantz, *Public Health and Medicine’s Need to Respond to Marijuana Commercialization in the United States: A Commentary*, JOURNAL OF PSYCHOACTIVE DRUGS, 1–6 (2020); J. Marcu, *Regulators Need to Rethink Restrictions on Marijuana Research*, NATURE, 572, S19–S19 (2019); Russo EB, Mead AP, Sulak D., *Current Status and Future of Marijuana Research*, CLINICAL RESEARCHER, 58-63 (April 2015); A. Mead, *The Legal Status of Marijuana (Marijuana) and Cannabidiol (CBD) Under U.S. Law*, EPILEPSY & BEHAVIOR, 70, 288-91, (May 2017); A. Mead, *Legal and Regulatory Issues Governing Marijuana and Marijuana-Derived Products in the United States*, FRONT PLANT SCIENCE, 10, 697 (2019); *See United States v. McIntosh*, 833 F.3d 1163, 1178 (9th Cir. 2016) (prohibiting prosecution of individuals engaged in activity authorized by state marijuana laws).

settled expectations and the reliance interests that have arisen as a result of the Cole Memoranda.”)

No medical institution that receives or seeks federal funding is willing to sponsor and undertake the high-quality clinical studies of marijuana the DEA and FDA demand because of the significant risk and catastrophic consequence of losing the many streams of federal funding on which they rely. Hospitals cannot afford to jeopardize the Medicare, Medicaid, and many other streams of federal funds they receive by engaging in clinical research activity that requires them to procure and dispense a Schedule I drug in violation of the CSA.

Likewise, colleges and universities cannot afford to sponsor this research and risk losing the billions of dollars in research grants, student financial aid, and other forms of federal financial assistance upon which they rely. Moreover, most research hospitals and research universities are 501(c)(3) nonprofit organizations that cannot afford to jeopardize the tax-exempt status of their institutions by allowing researchers to properly evaluate the medical efficacy and safety of marijuana.

Moreover, approximately 80 million Americans, about 25 percent of the U.S. population, live in a state where marijuana is legal for medical and adult-use purposes.⁹ Over two-thirds of Americans, roughly 225 million people, live in a state with legalized

⁹ <https://www.washingtonpost.com/business/2018/11/07/michigan-becomes-th-state-allow-recreational-marijuana/>.

medical access.¹⁰ These figures are likely to increase by 2021, as several states have medical and adult-use legalization initiatives on their November 2020 ballots.¹¹ Support for legalization of medical marijuana is overwhelming; the latest Pew Research poll found that 91 percent of Americans approve of legalizing marijuana for medical use.¹² 59 percent of Americans say marijuana should be legal for general adult use.¹³

Gary Hale, a 31-year DEA veteran who retired in 2010 after serving nine years as Chief of intelligence in the Houston field division of the DEA, writing in the *Houston Chronicle* about the incongruity of the placement of marijuana in Schedule I, observed: “The agency in which I worked for 31 years, many of them at a high level, must accept that the American people simply do not wish to have our federal government continue to spend time, money and resources fighting marijuana possession and use, especially in light of convincing evidence that marijuana provides alternative medicinal choices for epileptics, veterans with post-traumatic stress disorder, those suffering the pains of cancer and others.”¹⁴

¹⁰ <https://www.pewresearch.org/fact-tank/2019/11/14/americans-support-marijuana-legalization/>.

¹¹ <https://www.mpp.org/policy/ballot-initiatives/>.

¹² <https://www.pewresearch.org/fact-tank/2019/11/14/americans-support-marijuana-legalization/>.

¹³ <https://www.pewresearch.org/fact-tank/2019/11/14/americans-support-marijuana-legalization/>.

¹⁴ <https://www.houstonchronicle.com/opinion/outlook/article/Gary-Hale-Pot-legalization-is-no-longer-a-trend-5626411.php>.

The change in attitudes—and the growing acknowledgement that marijuana has therapeutic value in the United States—is part of a growing global trend. Canada, Mexico, Germany, France, Greece, Portugal, South Korea, Australia, South Africa, Argentina, Chile, and 29 other countries allow for medical access to marijuana.¹⁵

It is time the DEA caught up with its own government, the States, the World Health Organization, and other countries to consider the already medically accepted uses by removing marijuana from its untenable status as a Schedule I substance and allowing research of the plant.

II. Scientific Data Demonstrates Marijuana’s Propensity to Treat Symptoms of Chronic Pain and PTSD, and to Combat the Opioid Epidemic

A. The Widespread Harms of Untreated Pain

Chronic pain, defined as lasting longer than six months, is debilitating and difficult to treat.¹⁶ The Institute of Medicine estimated “more than 100 million Americans suffer from chronic pain,”¹⁷ that the annual direct and indirect costs of untreated chronic pain totals \$560-\$635 billion, and more Americans suffer from

¹⁵ See The Cannigma Staff, *Marijuana Regulation Around the World* (Oct. 2, 2019), <https://cannigma.com/regulation/marijuana-regulation-around-the-world/#central-south-america>.

¹⁶ The Cleveland Clinic, 2017, “Acute vs. Chronic Pain,” <https://my.clevelandclinic.org/health/articles/12051-acute-vs-chronic-pain>.

¹⁷ 100 Million have chronic pain. <https://wb.md/2FsaDHW>.

chronic pain conditions than heart disease, cancer, and diabetes combined.¹⁸ Chronic pain may also induce depression.¹⁹

Untreated chronic pain contributes to opioid and alcohol misuse and to the overdose epidemic.²⁰ According to the National Survey on Drug Use and Health, 9.9 million Americans aged 12 and older misused prescription pain killers in 2018.²¹ When asked their primary reason for that misuse, 63.6 percent of respondents said it was to “relieve physical pain.”²²

Misuse of prescription pain killers increases the risk of developing a substance use disorder (SUD) and overdosing. Nearly 1.7 million people had a SUD involving a prescription pain reliever in 2018, and in 2019, there were an estimated 72,707 drug overdose deaths, approximately 50,000 of which involved an opioid.²³

¹⁸ *Id.*

¹⁹ Sheng, J., et al., 2017, “The Link between Depression and Chronic Pain: Neural Mechanisms in the Brain,” *Neural Plasticity*, <https://psycnet.apa.org/record/2017-27829-001>.

²⁰ Witkiewitz, K., & Vowles, K.E., 2018, “Alcohol and Opioid Use, Co-Use, and Chronic Pain in the Context of the Opioid Epidemic: A Critical Review,” *Alcoholism Clinical & Experimental Research*, 42(3), 478-488, https://onlinelibrary.wiley.com/doi/full/10.1111/acer.13594?casa_token=5l-m3nCWwr4AAAAA%3AGT2q2K_GmQHwJ2TLQ0QgCp9gxN8lJnJZBZ7Vsh6WiRZEO2Ef5l5khFLyDuNy0sNX-JHzLGmzm7n2xA.

²¹ 2018 National Survey on Drug Use and Health: Detailed Tables, Substance Abuse and Mental Health Services Administration, <https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables>.

²² 2018 National Survey on Drug Use and Health: Detailed Tables, Substance Abuse and Mental Health Services Administration, <https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables>.

²³ 2018 National Survey on Drug Use and Health: Detailed Tables, Substance Abuse and Mental Health Services Administration, <https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables>; National Center for Health statistics, 2020, *Provisional Drug Overdose Death Counts*, Centers for Disease

B. Implications for Marijuana’s Potential to Alleviate Pain and Reduce Opioid Use

Marijuana and cannabinoids have an established ability to diminish chronic pain.²⁴ For acute pain such as that from surgery, burns, broken bones, or advanced cancer, cannabinoids alone are often insufficient.²⁵ However, there is some evidence suggesting that, used in combination with opioids, they could reduce the amounts needed for acute pain and thereby lessen the chance of overdose.²⁶ Studies have also shown that statewide opioid prescribing tends to decrease following passage of medical marijuana legislation.²⁷

For chronic pain, a review of evidence carried out by the National Academies of Science, Engineering, and Medicine found “substantial evidence” from clinical trials that cannabinoids (mainly THC or THC and CBD) can help relieve chronic pain –

Control and Prevention, https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm#COD_classification_definition_drug_deaths.

²⁴ Nielsen, Suzanne, et al. "Opioid-sparing effect of cannabinoids: a systematic review and meta-analysis." *Neuropsychopharmacology* 42.9 (2017): 1752-1765.

²⁵ Stevens, A. J., and M. D. Higgins. "A systematic review of the analgesic efficacy of cannabinoid medications in the management of acute pain." *Acta Anaesthesiologica Scandinavica* 61.3 (2017): 268-280.

²⁶ <https://drugabuse.com/legalizing-marijuana-decreases-fatal-opiate-overdoses/>.

²⁷ Bradford AC, Bradford WD. Medical Marijuana Laws Reduce Prescription Medication Use In Medicare Part D. *Health Aff (Millwood)* 2016;35:1230-6; Bradford AC, Bradford WD. Medical Marijuana Laws May Be Associated With A Decline In The Number Of Prescriptions For Medicaid Enrollees. *Health Aff (Millwood)* 2017;36:945-51; Bradford AC, Bradford WD, Abraham A, Bagwell Adams G. Association Between US State Medical Marijuana Laws and Opioid Prescribing in the Medicare Part D Population. *JAMA Intern Med* 2018;178:667-72.

mostly of neuropathic origin.²⁸ This report highlighted research barriers (most notably: marijuana’s Schedule I status) that prevented effective understanding of marijuana as medicine.

Marijuana’s ability to alleviate chronic pain and reduce reliance on opioids has far-reaching implications. Numerous studies have found that “when given access to marijuana, individuals currently using opioids for chronic pain decrease their use of opioids by 40–60 percent and report that they prefer marijuana to opioids,” reporting fewer side effects, better symptom management, and a better quality of life.²⁹ These studies have been conducted throughout the U.S. as well as in Canada and Israel.³⁰

²⁸ The National Academies of Sciences, Engineering, and Medicine, 2017, *The Health Effects of Marijuana and Cannabinoids*, <https://www.nap.edu/catalog/24625/the-health-effects-of-marijuana-and-cannabinoids-the-current-state>.

²⁹ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6135562/#B36>.

³⁰ Boehnke KF, Litinas E, Clauw DJ. Medical Marijuana Use Is Associated With Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients With Chronic Pain. *J Pain* 2016;17:739-44; Boehnke KF, Scott JR, Litinas E, Sisley S, Williams DA, Clauw DJ. Pills to Pot: Observational Analyses of Marijuana Substitution Among Medical Marijuana Users With Chronic Pain. *J Pain* 2019;20:830-41; Reiman A, Welty M, Solomon P. Marijuana as a Substitute for Opioid-Based Pain Medication: Patient Self-Report. *Marijuana Cannabinoid Res* 2017;2:160-6; 1; Lucas P, Walsh Z, Crosby K, et al. Substituting marijuana for prescription drugs, alcohol and other substances among medical marijuana patients: The impact of contextual factors. *Drug Alcohol Rev* 2016;35:326-33; Lucas P, Walsh Z. Medical marijuana access, use, and substitution for prescription opioids and other substances: A survey of authorized medical marijuana patients. *Int J Drug Policy* 2017;42:30-5; Baron EP, Lucas P, Eades J, Hogue O. Patterns of medicinal marijuana use, strain analysis, and substitution effect among patients with migraine, headache, arthritis, and chronic pain in a medicinal marijuana cohort. *J Headache Pain* 2018;19:37; Lucas P, Baron EP, Jikomes N. Medical marijuana patterns of use and substitution for opioids & other pharmaceutical drugs, alcohol, tobacco, and illicit substances; results from a cross-sectional survey of authorized patients. *Harm Reduct J* 2019;16:9; Abuhassira R, Schleider LB, Mechoulam R, Novack V. Epidemiological characteristics, safety and efficacy of medical marijuana in the elderly. *Eur J Intern Med* 2018;49:44-50; Bar-Lev Schleider L, Mechoulam R, Lederman V, et al. Prospective analysis of safety and efficacy of medical marijuana in large unselected population of patients with cancer. *Eur J Intern Med* 2018;49:37-43; Sagy I, Bar-Lev

Moreover, the risks of using opioids for chronic pain management often outweighs the potential benefits, demonstrated by CDC guidelines suggesting that opioids should only be used after all other options have failed and only when benefits outweigh risks.³¹

Additionally, given the widespread use of marijuana among veterans for PTSD symptoms, and their concurrent experience with chronic pain and over-prescription of opioids to treat those symptoms, there is a great need to understand how best to effectively use marijuana for PTSD symptom management, especially as there is evidence of cannabinoid efficacy for treating some common PTSD symptoms (*e.g.*, pain, sleep disturbances). Unfortunately, the scientific literature has been effectively limited by research barriers that have resulted in few rigorous studies of marijuana in PTSD. While there are several ongoing PTSD clinical trials using herbal cannabis and synthetic cannabinoids, these trials cannot use products currently available in medical cannabis dispensaries. Dr. Sisley's research would be crucial in this regard.

To summarize, millions of Americans suffer from chronic pain. Prescription opioids can reduce pain for some individuals, but are generally not appropriate for

Schleider L, Abu-Shakra M, Novack V. Safety and Efficacy of Medical Marijuana in Fibromyalgia. *J Clin Med* 2019; 8; Naftali T, Bar-Lev Schleider L, Sklerovsky Benjaminov F, Lish I, Konikoff FM, Ringel Y. Medical marijuana for inflammatory bowel disease: real-life experience of mode of consumption and assessment of side-effects. *Eur J Gastroenterol Hepatol* 2019;31:1376-81.

³¹ Collen, M., 2012, "Prescribing Marijuana for Harm Reduction," *Harm Reduction Journal*, 9, <https://link.springer.com/article/10.1186/1477-7517-9-1>; Dowell, Deborah, Tamara M. Haegerich, and Roger Chou. "CDC guideline for prescribing opioids for chronic pain—United States, 2016." *JAMA* 315.15 (2016): 1624-1645.

chronic pain management as long-term opioid use can lead to depression and addiction, and they have contributed heavily to the current opioid crisis. In contrast, marijuana can alleviate chronic pain in some cases, and while it does carry some risks (intoxication, behavioral disturbances, dependence), marijuana is not known to cause lethal overdoses. As such, marijuana and cannabinoids represent an alternative to opioids for chronic pain management that scientists should be allowed to study to best determine how to maximize benefits and minimize harm among people using marijuana in this context.

C. Marijuana’s Relationship with Substance Use Disorders and Other Drug Use

Emerging evidence suggests that marijuana may help reduce illicit opioid use or help wean people off of opioids. Recent research conducted in Vancouver, Canada, and published in *PLOS Medicine* found that among people who use drugs and have chronic pain, illicit opioid use was lower among daily marijuana users.³² This is consistent with previous research finding that people who inject drugs and also use marijuana report significantly less frequent opioid use compared to people who inject drugs and do not use marijuana.³³ Other studies indicate that cannabinoids can ease symptoms

³² Lake, S. Walsh, Z., Kerr, T., Cooper, Z.D., Buxton, J., Wood, E., Ware, M.A., & Milloy, M.J., 2019, Frequency of Marijuana and Illicit Opioid Use among People Who Use Drugs and Report Chronic Pain: A Longitudinal Analysis,” *PLOS Medicine*, <https://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002967>.

³³ Kral, A.H., Wenger, L, Novak, S.P., Chu, D., Corsi, K.F., Coffa, D., Shapiro, B., Bluthenthal, R.N., 2015, “Is Marijuana Use Associated with Less Opioid Use Among People Who Inject Drugs?” *Drug and Alcohol Dependence*, 153, 236-241,

experienced during opioid withdrawal, a necessary precursor to starting an opioid antagonist therapy such as naltrexone.³⁴ A randomized control trial involving dronabinol, the FDA-approved synthetic version of THC, found that patients receiving the dronabinol experienced less severe opioid withdrawal symptoms.³⁵ Similarly, another study showed that compared to placebo, CBD reduced cue-induced craving and anxiety among participants recovering from heroin addiction.³⁶ A study of opioid dependent patients that were being treated with oral naltrexone found intermittent marijuana use to be associated with significantly improved treatment retention rates.³⁷

https://www.sciencedirect.com/science/article/pii/S0376871615002501?casa_token=7UO_w3pL9IQAAAAA:nSlMoPu6DMfIMh3e2Tt_x2tudVQeudfic55WpZBm9Q8JtsplhbRs0jymkkNzyFgyVzI2d07i2A.

³⁴ Wiese, B., & Wilson-Poe, A.R., 2018, “Emerging Evidence for Marijuana’ Role in Opioid Use Disorder,” *Marijuana and Cannabinoid Research* 3(1), <https://www.liebertpub.com/doi/full/10.1089/can.2018.0022>; American Society of Addiction Medicine, The National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use, <https://www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asam-national-practice-guideline-supplement.pdf>.

³⁵ Bisaga, A., Sullivan, M.A., Glass, A., Mishlen, K., Paclivova, M., Haney, M., Raby, W.N., Levin, F.R., Carpenter, K.M., Mariani, J., & Nunes, E. V., 2015, “The Effects of Dronabinol during Detoxification and the Initiation of Treatment with Extended Release Naltrexone,” *Drug and Alcohol Dependence*, 154: 38-45, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4536087/#:~:text=Dronabinol%20reduced%20the%20severity%20of,regardless%20of%20treatment%20group%20assignment>.

³⁶ Boehnke KF, Scott JR, Litinas E, et al. Marijuana Use Preferences and Decision-making Among a Cross-sectional Cohort of Medical Marijuana Patients with Chronic Pain. *J Pain* 2019;20:1362-72.

³⁷ Raby, W.N., 2009, “Intermittent Marijuana Use is Associated with Improved Retention in Naltrexone Treatment for Opiate-Dependence,” *American Journal of Addiction*, 18 (4), 301-308, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2753886/>. Oral naltrexone is an opioid antagonist that prevents a person from experiencing opioids’ effects by blocking the brain’s opioid receptors; it must be taken every day and thus often has limited effectiveness due to lack of treatment adherence.

While most of these studies were uncontrolled and are not definitive, they highlight a trend that warrants further study.

Preliminary studies also demonstrate marijuana's potential efficacy in addressing other substance use issues.³⁸ The Summer 2017 issue of *Neuroscience Quarterly* reported CBD can significantly reduce preference for alcohol in mice.³⁹ Similarly, surveys have shown that up to twenty-five percent of Canadian marijuana users self-reported substituting marijuana for alcohol.⁴⁰ Approximately 14.8 million Americans had an alcohol use disorder in 2018, so reductions of that magnitude may have significant public health benefits.⁴¹ A scoping review published in March 2020 that included 57 articles in 33 countries found marijuana can enhance the pain management properties of prescription opioids and reduce dependence on opioids, cocaine, alcohol, and nicotine, and that these benefits can be gained through routes of administration other than smoking, such as vaporizing and ingesting marijuana.⁴² While these results suggest

³⁸ Risso, Constanza, et al. "Does cannabis complement or substitute alcohol consumption? A systematic review of human and animal studies." *Journal of Psychopharmacology* 34.9 (2020): 938-954.

³⁹ *Neuroscience Quarterly*, 2017, "Inside Neuroscience: Tapping into the Cannabinoid System," <http://bit.ly/2HIIft8>.

⁴⁰ Lucas & Walsh, "Medical Marijuana Use."

⁴¹ 2018 National Survey on Drug Use and Health: Detailed Tables, Substance Abuse and Mental Health Services Administration, <https://www.samhsa.gov/data/report/2018-nsduh-detailed-tables>; Neill Harris, K., & Martin, W., 2020, *Vaping: Clearing the Air*, Baker Institute Report.

⁴² Siklos, Whillans, J., Bacchus, A., & Manwell, L.A., 2020, "A Scoping Review of the Use of Marijuana and Its Extracts as Potential Harm Reduction Strategies: Insights from Preclinical and Clinical Research," *International Journal of Mental Health and Addiction*, <https://link.springer.com/article/10.1007%2Fs11469-020-00244-w#citeas>.

great promise, the lack of controlled studies highlights how important marijuana research is to understand the populations in which this substitution is occurring and how to monitor the substitution in a judicious way.

Research to date suggests that marijuana can potentially address unmet health problems that many people attempt to alleviate through other pharmacological means, both licit and illicit, some of which carry significant risks.⁴³ To judiciously approach the complex issue of addiction—especially given that marijuana itself can be addictive—there is a dire need for future research with rigorous control and selection criteria that examines variations in marijuana’s effects that may be dependent on route of administration, cannabinoid concentrations, and dose.⁴⁴

D. Harms Caused by Research Restrictions

Legalization of medical marijuana is rapidly progressing across the country.⁴⁵ Over two-thirds of the US population lives in a state where medicinal marijuana is legal,

⁴³ Benzodiazepines, for example, a commonly prescribed class of sedatives, are increasingly implicated in overdose deaths and have dependence potential, Kang, M., Galuska, M.A., & Ghassemzadeh, S., 2020, “Benzodiazepine Toxicity,” StatPearls Publishing, <https://www.ncbi.nlm.nih.gov/books/NBK482238/>; National Institute on Drug Abuse, 2018, “Benzodiazepines and Opioids,” <https://www.drugabuse.gov/drug-topics/opioids/benzodiazepines-opioids>.

⁴⁴ Siklos et al., “A Scoping Review of the Use of Marijuana;” Volkow, Nora D., et al. "Adverse health effects of marijuana use." *New England Journal of Medicine* 370.23 (2014): 2219-2227.

⁴⁵ See National Conference of State Legislatures, 2020, “State Medical Marijuana Laws,” March 10, <https://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx>.

and there are an estimated 4.38 million medical marijuana patients in the U.S.⁴⁶ Yet, marijuana is still considered by the DEA to have “no currently accepted medical use and a high potential for abuse.”⁴⁷ This outdated justification perpetuates daunting research restrictions, leading to a critical mismatch between knowledge and practice, in which millions of Americans consume a psychoactive substance with relatively little guidance regarding safe use, proper dosage, possible interactions with other medications and medical conditions, and long-term effects.⁴⁸

Currently allowed research is typically narrow in scope and must be conducted using unrepresentative marijuana.⁴⁹ However, marijuana is increasingly consumed through vaporizing, tinctures, concentrates and edibles. The health effects of these newer routes of administration are less known, and there is concern that highly potent products (e.g., concentrates) could have unknown negative side effects. The DEA’s restrictions on marijuana hamper insight into that agency’s chief concern, marijuana’s harms. Further, while research into marijuana’s therapeutic properties has been blocked, NIH funding to investigate harms from marijuana is over *twenty-fold higher* than what is

⁴⁶ Marijuana Policy Project, 2020, “Medical Marijuana Patient Numbers,” July 6, <https://www.mpp.org/issues/medical-marijuana/state-by-state-medical-marijuana-laws/medical-marijuana-patient-numbers/>.

⁴⁷ Drug Enforcement Administration, “Drug Scheduling,” <https://www.dea.gov/drug-scheduling#:~:text=Schedule%20I%20drugs%2C%20substances%2C%20or,Schedule%20II>.

⁴⁸ https://www.fda.gov/news-events/public-health-focus/fda-and-marijuana-research-and-drug-approval-process_2018 National Survey on Drug Use and Health; Lucas & Walsh; Cooke et al.

⁴⁹ <https://cen.acs.org/biological-chemistry/natural-products/Marijuana-research-stalled-federal-inaction/98/i25>.

spent on therapeutic research, according to an analysis of marijuana research grants from 50 public agency and charity funders—untenably justified in 2020 when pain management alternatives are desperately needed.⁵⁰

Research restrictions also mean the U.S. now lags behind other Western nations in this critical area of scientific inquiry.⁵¹ Limitations and “red tape” in the study approval process create significant obstacles that discourage talented researchers from pursuing important marijuana research. Clinical trials involving human subjects, considered the gold standard of medical research, are especially difficult to implement.⁵² Instead, U.S. companies interested in marijuana research outsource it to other countries, primarily Israel, where research has government support.⁵³ The National Institutes of Health, a U.S. government organization, funds medicinal marijuana research in Israel.⁵⁴

The lack of research causes significant public harm, as trends in use have outpaced scientific inquiry. For example, a study of individuals with chronic non-cancer pain found that it was common for patients receiving opioids for pain management to

⁵⁰ <https://www.sciencemag.org/news/2020/08/marijuana-research-database-shows-how-us-funding-focuses-harms-drug>.

⁵¹ <https://www.usnews.com/news/best-countries/articles/2017-04-11/israel-is-a-global-leader-in-marijuana-research>; <https://www.analyticalmarijuana.com/articles/inside-the-clinical-trials-using-marijuana-for-cancer-treatments-311737>.

⁵² *Ibid.*

⁵³ <https://www.usnews.com/news/best-countries/articles/2017-04-11/israel-is-a-global-leader-in-marijuana-research>.

⁵⁴ *Ibid.*

supplement their prescribed medication regimen with marijuana,⁵⁵ and patients often report using multiple administration routes (smoking, vaping, edibles, etc.) and various CBD:THC ratios in combination with many medications.⁵⁶ While patients reported benefits from marijuana use, both patients and clinicians consistently point to a lack of knowledge and evidence-based guidance regarding the effects of dual use of marijuana and opioids.⁵⁷ The study authors conclude that marijuana’s federal classification as a Schedule I substance “contributes to the lack of scientific evidence on marijuana that could inform clinicians about dosing clinical efficacy, routes of administration, and contraindications.”⁵⁸

The plant’s complexities and effects that vary with potency, route of administration, and individual physical/psychological characteristics, combined with

⁵⁵ Cooke, A.C., Knight, K.R., & Miaskowski, C., 2019, “Patients’ and Clinicians’ Perspectives of Co-Use of Marijuana and Opioids for Chronic Non-Cancer Pain Management in Primary Care,” *International Journal of Drug Policy*, 63, 23-28, https://www.sciencedirect.com/science/article/pii/S0955395918302287?casa_token=69rTLOCdm iwAAAAA:vo89tMv4rJ76pbpq6gJz89FfIZ73AEnOpqQYe1FA2q4PuEO3o_ZsITfpRf1XXhR6ZXcAyokCA.

⁵⁶ Boehnke KF, Scott JR, Litinas E, et al. Marijuana Use Preferences and Decision-making Among a Cross-sectional Cohort of Medical Marijuana Patients with Chronic Pain. *J Pain* 2019; 20:1362-72.

⁵⁷ Cooke *et al.*

⁵⁸ Cooke *et al.*, *See also* Maher, D.P., Carr, D.B., Hill, K., McGeeney, B., Weed, V., Jackson, W.C., DiBenedetto, D.J., Moriarty, E., & Kulich, R.J., 2017, “Marijuana for the Treatment of Chronic Pain in the Era of an Opioid Epidemic: A Symposium-Based Review of Sociomedical Science,” *Pain Medicine*, 20(11), 2311-2323, <https://academic.oup.com/painmedicine/article-abstract/20/11/2311/3964518?redirectedFrom=PDF>

See Campbell, G., Hall, W., & Nielsen, S., 2018, “What does the Ecological and Epidemiological Evidence Indicate about the Potential for Cannabinoids to Reduce Opioid Use and Harms? A Comprehensive Review,” *International Review of Psychiatry*, 20(55), 91-106, <https://www.tandfonline.com/doi/abs/10.1080/09540261.2018.1509842>.

the fact that millions of people legally consume it, demands research to understand these effects. By imposing research restrictions, the federal government is actively blocking the development of well-informed public policies and medical guidelines regarding marijuana use to protect the health and safety of the American citizenry.

In its letter to Mr. Zyszkiewicz, the DEA states it will “never los[e] sight of the need to protect the public.”⁵⁹ The DEA’s preferred method for protecting the public from drugs has been to reduce their supply. Given the widespread availability and increasingly legal use of marijuana, it is reasonable to conclude that the DEA has failed in this mission. Continued resistance to advancing research, predicated on the notion that there is enough evidence of marijuana’s dangers and not enough evidence of its benefits to warrant further study, does not protect the public but in fact harms it by obstructing insight into the health effects of an activity that 45 percent of Americans over the age of 12 have done at least once in their lifetime.⁶⁰ Moreover, the harms of the criminalization of marijuana include an average of more than 622,000 arrests in the past three years which result in massive individual, community, and societal trauma.

⁵⁹ Case No. 20-71433, *Sisley v. U.S. Drug Enforcement Administration, et al.*, 5/21/2020, ID: 11698131, DktEntry: 1-6, Page 25 of 203 (Ex. 2, Letter from DEA to Stephen Zyszkiewicz (undated)).

⁶⁰ NSDUH 2018.

E. Public Policy Demands Advances Allowing Research

Allowing more research on marijuana’s health effects is critical to helping policymakers make informed decisions about how to properly regulate marijuana products and how to balance competing priorities of allowing access to people who can benefit from marijuana use while discouraging use among youth and others for whom marijuana use might have negative impacts.⁶¹ Research that addresses gaps in knowledge about marijuana can also provide guidance to health care professionals and can aid public education efforts that are intended to educate the public about the health effects of marijuana use.⁶²

The U.S. government also stands to benefit from allowing more marijuana research. Providing citizens with accurate and evidence-based information about a substance that is commonly consumed is a critical part to fulfilling the government’s role of supporting the health and safety of its citizens.

One of the many collateral consequences of the War on Drugs is that a large segment of the American public distrusts the intent of U.S. drug policy and the information on drug use that the government provides. Regarding marijuana specifically, government misinformation in the style of “Reefer Madness,” as well as revelations that enforcement of marijuana prohibition historically was intended to target

⁶¹ Siklos et al., “Scoping Review of Marijuana for Harm Reduction.”

⁶² Siklos et al., “Scoping Review of Marijuana for Harm Reduction.”

minorities, has resulted in widespread and deep-seated mistrust of government. The DEA's assertions that marijuana has no established medical benefits and high abuse potential is inconsistent with scientific evidence from the 2017 National Academies of Sciences, Engineering, and Medicine report on this topic.

While many people who consume marijuana do not experience serious adverse effects, research would illustrate what causes adverse effects and who is at risk for problematic marijuana use versus who would benefit from it.⁶³ But a sizable portion of the public, and perhaps especially those who are more inclined to marijuana use, see the government's resistance to research as indicative of its anti-marijuana bias and evidence that its claims about marijuana cannot be trusted.⁶⁴ Attempts by the government to educate the public on marijuana's harms, then, often fall on deaf ears. Allowing more research could help rebuild public trust by demonstrating a sincere desire to craft drug policies that are grounded in scientific evidence and designed to advance public health.

In addition to improving the public's and medical practitioner's marijuana knowledge base, advancements in medical marijuana could be fiscally advantageous as well. For example, the use of prescription opioids dropped by more than 3.7 million

⁶³ Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. *N Engl J Med* 2014;370:2219-27; Volkow ND, Swanson JM, Evins AE, et al. Effects of Marijuana Use on Human Behavior, Including Cognition, Motivation, and Psychosis: A Review. *JAMA Psychiatry* 2016;73:292-7.

⁶⁴ Keyhani, Salomeh, et al. "Risks and benefits of marijuana use: a national survey of US adults." *Annals of Internal Medicine* 169.5 (2018): 282-290.

daily doses among Medicare D enrollees from 2007 to 2014 in states with legal medical marijuana,⁶⁵ the authors estimated that if all states legalized medical marijuana, the savings to Medicare in 2014 would be \$468 million.⁶⁶ Similarly, a 2018 paper examining Medicaid data estimated that all-states medical legalization would produce national savings for fee-to-service Medicaid of \$1.01 billion; if Medicaid managed care were included, the estimated savings would be \$3.89 billion.⁶⁷ A 2019 study concluded that smoked marijuana could be cost-effective as a second line therapy for chronic neuropathic pain.⁶⁸ While inconclusive at this time, these suggestive studies highlight the potential cost-savings associated with effectively harnessing cannabis's therapeutic benefits.

CONCLUSION

Policy experts, scientists, researchers, and physicians all agree that marijuana has demonstrated therapeutic potential and should be further researched without delay or undue restriction. The only entity that disagrees, and that has been the source of decades of impeded research, which quite possibly has resulted in the suffering of millions that

⁶⁵ Ashley and David Bradford Medicare study. <http://bit.ly/2CyAVpX>.

⁶⁶ Ashley and David Bradford Medicare study. <http://bit.ly/2CyAVpX>.

⁶⁷ Ashley C. Bradford, et al., "Association Between US State Medical Marijuana Laws and Opioid Prescribing in the Medicare Part D Population," *JAMA Internal Medicine*, 2018; DOI: 10.1001/jamainternmed.2018.0266.

⁶⁸ Tyree, Griffin A., et al. "A Cost-Effectiveness Model for Adjunctive Smoked Marijuana in the Treatment of Chronic Neuropathic Pain." *Marijuana and cannabinoid research* 4.1 (2019): 62-72.

could have been avoided or reduced, is the DEA. As recounted herein from a legal, public policy, and scientific perspective, the continued inconsistency in federal policy and federal and state law cannot be tolerated any longer. DEA can no longer rest on outdated conclusions to continue to summarily reject all petitions to remove marijuana from Schedule I, and, to continue to take no action on allowing the research on the therapeutic potential of marijuana.

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Respectfully submitted,

COATS ROSE, PC
Terrace Two
2700 Via Fortuna, Suite 350
Austin, Texas 78746-7911
Telephone 512.469.7987
Facsimile 512.469.9408
lpittman@coatsrose.com

By: /s/Lisa L. Pittman
Lisa L. Pittman

STATEMENT OF RELATED CASES

Amici is not aware of related cases.

CERTIFICATE OF COMPLIANCE

I am the attorney or self-represented party.

This brief contains 4549 words, excluding the items exempted by Fed. R. App. P. 32(f). The brief's type size and typeface comply with Fed. R. App. P. 32(a)(5) and (6).

I certify that this brief is an amicus brief and complies with the word limit of Fed. R. App. P. 29(a)(5), Cir. R. 29-2(c)(2), or Cir. R. 29-2(c)(3).

Signature /s/ Lisa L. Pittman

Date October 6, 2020

CERTIFICATE OF SERVICE

I hereby certify that I electronically filed this document with the Clerk of the Court for the United States Court of Appeals for the Ninth Circuit by using the appellate CM/ECF system on October 6, 2020. I certify that all participants in the case are registered CM/ECF users and that service will be accomplished by the appellate CM/ECF system.

Matthew C. Zorn
Shane Pennington
YETTER COLEMAN LLP
811 Main Street, Suite 4100
Houston, Texas 77002
(713) 632-8000
(713) 632-8002
mzorn@yettercoleman.com
spennington@yettercoleman.com

Attorneys for Petitioners

Mark B. Stern
Daniel Aguilar
Attorneys, Appellate Staff
Civil Division, Room 7266
Department of Justice
950 Pennsylvania, NW
Washington, DC 20530

Counsel for Respondents

Erica W. Harris
Susman Godfrey L.L.P.
1000 Louisiana Street, Suite 5100
Houston, Texas 77002-5096

*Counsel for Amicus Iraq and Afghanistan
Veterans of America*

/s/ Lisa L. Pittman

Lisa L. Pittman