

Headquartered at UC San Diego

# Center for Medicinal Cannabis Research Has 18 State-Funded Studies in the Pipeline

By Dale Gieringer

While U.S. government drug bureaucrats are loudly demanding rigorous scientific evidence for the medical efficacy of marijuana, the California Center for Medicinal Cannabis Research is quietly sponsoring an ambitious program of controlled clinical studies to help shed light on the issue.

The CMCR, headquartered at the University of California San Diego, now has 14 clinical studies of medical cannabis under way, plus four more undergoing review by regulatory authorities. Included are the first human efficacy studies of smoked natural cannabis for medical purposes since such research was shut down by the Reagan administration in the early 1980s.

The CMCR was established by the state legislature under the Marijuana Research Act of 1999. The act was sponsored by Sen. John Vasconcellos with support from former Attorney General Dan Lungren, a leading opponent of Prop. 215, on the grounds that more research was needed on the medical value of marijuana. Under the act, the CMCR was directed to “develop and conduct studies to ascertain the general medical safety and efficacy of marijuana and, if found valuable ...[to] develop medical guidelines for the appropriate administration and use of marijuana.”

CMCR researchers are currently conducting placebo-controlled efficacy studies of smoked cannabis for treatment of HIV-related peripheral neuropathy, spasticity and tremors due to multiple sclerosis, and cancer pain and nausea. The cannabis used in the study is grown in Mississippi under license from the Drug Enforcement Administration and provided to the researchers by the National Institute on Drug Abuse

In one study, Dr. Donald Abrams of

UCSF is examining the combination of cannabis with opiates for treatment of cancer pain. In another, Suzanne Dibble of UCSF is comparing smoked cannabis, oral Marinol, and smoked and oral placebos in the treatment of nausea from cancer chemotherapy. Other CMCR investigators are examining the effects of cannabis on driving ability, sleeping patterns, and artificially induced pain and neuropathy.

The CMCR has also approved groundbreaking studies on two new modes of cannabis administration: vaporization and an oral cannabis spray. The FDA has given approval for what would be the first-ever human trial using a cannabis vaporizer, the Volcano® (<http://www.vapormed.de>), in a dosage study of healthy subjects by Abrams.

The FDA has also approved the first U.S. study of an oral cannabis extract manufactured by GW Pharmaceuticals (<http://www.gwpharm.com>), a British company whose product may be approved this spring by U.K. authorities. The study, by Dr. Ronald Ellis of UCSD, will examine patients with HIV neuropathic pain. Both studies are still awaiting final DEA approval.

Several CMCR studies are aimed at uncovering the basic mechanisms through which cannabinoids achieve their effects within the body. Daniele Piomelli of UCSD is trying to determine the impact of external cannabinoids — smoked or otherwise ingested — on the body’s own endogenous cannabinoid system. Piomelli’s hypothesis is that

“long-term cannabis and THC administration interfere with activity of the endocannabinoid system.”

Piomelli’s group will use a technique called high performance liquid chromatography/mass spectrometry to test blood plasma samples obtained from patients in a CMCR clinical study. They expect the introduction of smoked cannabis to decrease the rate at which natural, fat-derived endocannabinoid compounds are produced, circulate, and/or interact with receptors.

“Brain neurotransmitter systems are highly plastic and regulate their activity when they are challenged with exogenous drugs,” writes Piomelli. “We hypothesize that treatment with cannabis or D 9-THC may produce compensatory changes in the activity of the endocannabinoid system. Such changes might in turn influence in important ways the therapeutic outcome of cannabinoid therapy and participate in withdrawal phenomena after drug cessation.”

### Abrams’s First Study Published

So far, only one CMCR study has released published results. In a pilot study of patients with HIV-related peripheral neuropathy, Dr. Donald Abrams found that 10 out of 16 subjects reported a greater than 30% reduction in pain after seven days of treatment. Based on these promising results, Dr. Abrams is proceeding with a randomized placebo-controlled trial with 50 subjects.

Researchers say it will be a year or

*Researchers must entice AIDS and cancer patients to volunteer for studies in which they receive low-grade NIDA cannabis or placebo in a cloistered clinical setting.*

two before more study results become available. Progress has been slow on account of the rigors and regulatory delays of modern controlled clinical research. Every study must be reviewed and approved by a gamut of regulatory agencies: the FDA, DEA, NIDA, the California Research Advisory Panel and an institutional review board.

Unlike other, independent research entities that have been denied approval for medical cannabis research, the CMCR has enjoyed good relations with federal regulators at the DEA and NIDA. The DEA went so far as to issue a press release crowing about its approval of the first two research applications by CMCR researchers. Despite this, it still took nearly a year for NIDA’s cannabis to reach the hands of CMCR researchers.

Another problem delaying CMCR researchers has been the difficulty of recruiting human subjects. Given that high-grade cannabis is already widely available to patients in California under Prop. 215, researchers have been hard pressed to entice AIDS and cancer patients to volunteer for controlled studies in which they receive low-grade NIDA cannabis or placebo in a cloistered clinical setting. Recruitment has proceeded at a snail’s pace.

The CMCR was originally conceived as a three-year program. This year, the legislature voted to extend its mandate indefinitely. Its existing research program has been funded by legislative appropriations totaling \$8.75 million over the past three years. No further funding is expected until more study results are announced.

Should the CMCR studies confirm that cannabis does have medical efficacy — as widely expected by knowledgeable observers — government regulators may finally be forced to revise federal policy. DEA, NIDA and ONDCP officials have repeatedly claimed that controlled scientific studies are essential to changing the Schedule One status of marijuana.

In the words of former DEA Commissioner Asa Hutchinson, “The question of whether marijuana has any legitimate medical purpose should be determined by sound science and medicine.”

Speaking at the Commonwealth Club in San Francisco, Hutchinson boasted that his agency had authorized CMCR researchers to conduct safety and efficacy studies of medical marijuana. “The DEA realizes how important it is to keep listening to science,” Hutchinson assured his audience. The proof will be in the pudding.

Copyright 2014 by O’Shaughnessy’s. All rights reserved. Address reprint requests to [editor@beyondthc.com](mailto:editor@beyondthc.com)



Donald Abrams



Daniele Piomelli

### Lead Investigator, Affiliation, Title of Approved Study

- Donald Abrams, MD UCSF Cannabis for Treatment of HIV-Related Peripheral Neuropathy
- Donald Abrams, MD UCSF Cannabis in Combination With Opioids for Cancer Pain
- Mark Agius, MD UC Davis Cannabis for Spasticity/Tremor in MS: Placebo-controlled study
- Jody Corey-Bloom, MD UCSD Short-Term Effects of Cannabis Therapy on Spasticity in MS
- Suzanne L. Dibble, DNSc, RN UCSF Treating Chemotherapy-Induced Delay Nausea with Cannabinoids
- Sean Drummond, PhD UCSD Sleep and Medicinal Cannabis
- Ronald Ellis, MD, PhD UCSD Placebo-Controlled Double-Blind Trial of Medicinal Cannabis in Painful HIV Neuropathy
- Dennis Israelski, MD San Mateo County MMJ for HIV-associated DSPN: Adherence & Compliance Sub-study
- Thomas Marcotte, PhD UCSF Impact of Repeated Cannabis Treatments on Driving Abilities
- Ian Meng, PhD, UCSF Mechanisms of Cannabinoid Analgesia
- Daniele Piomelli, PhD UC Irvine Effects of Cannabis Therapy on Endogenous Cannabinoids
- Rachel Schrier, Effects of Medicinal Cannabis on CD4 Immunity in AIDS
- Mark Wallace, MD UCSD Analgesic Efficacy of Smoked Cannabis
- Barth Wilsey, MD UC Davis Double-Blind, Placebo Controlled Trial of Smoked Marijuana on Neuropathic Pain

### Studies Undergoing State and Federal Review

- Donald Abrams, MD UCSF Vaporization as a Smokeless Cannabis Delivery System
- Mark Barad, MD, PhD UCLA Cannabinoids in Fear Extinction
- Ronald J. Ellis, MD, PhD UCSD Placebo-Controlled, Double-Blind Trial of Cannabis-Based Medicine Extract (CBME) in Painful HIV Neuropathy
- Mark Wallace, MD UCSD Analgesic Efficacy of Smoked Cannabis in Refractory Cancer Pain