

## Trials and Tribulations:

### A Review of MAPS' Medical Marijuana Research

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For the past twenty-five years, MAPS has been at the forefront of marijuana research. Despite the setbacks that its medical marijuana research protocol has encountered, it's important to consider the ways that MAPS has pushed the envelope by bringing the need for marijuana research to the awareness of the broader culture.

MAPS has been working for the past two years to get government approval to conduct a study with Dr. Sue Sisley at the University of Arizona on the safety and effects of smoked or vaporized marijuana on 50 U.S. veterans with chronic, treatment-resistant posttraumatic stress disorder (PTSD). The protocol has consistently taken two steps forward and one step back because of the obstructionist tactics of two federal agencies—NIDA and the DEA. A redundant research review process and a stalwart marijuana monopoly have left the new study tangled up in red tape.

The study is extremely timely and relevant given the ineffectiveness of treatment options currently available for veterans returning from Iraq and Afghanistan with PTSD. At present, available PTSD treatments are limited to several psychological counseling options and a handful of pharmaceutical drugs. According to the Defense Centers of Excellence, a military organization that studies the psychological health of service members, strictly pharmacological approaches to treating PTSD include selective serotonin reuptake inhibitors (SSRIs) and other antidepressants. However, the organization acknowledges that neither conventional psychotherapy nor currently available pharmaceuticals can completely ameliorate the symptoms of those suffering from PTSD. Instead, they propose alternative (though not FDA-approved) treatment options such as acupuncture, yoga, and dietary supplements to lessen the effects of PTSD.

One of the best ways to help veterans is to listen to what they already know about the treatments that work best for them. There are very many individuals in states that allow medical marijuana who have found that it helps them

cope with the often-debilitating symptoms of PTSD, such as anxiety, depression, nightmares, and insomnia. Many of these patients have told their doctors that the primary reason they are seeking to use medical marijuana is to treat their PTSD. The perceived benefit that these individuals see from marijuana in treating their condition provides a strong incentive for MAPS to dedicate resources to exploring whether marijuana really can help them achieve a better quality of life.

In November 2010, in order to investigate medical marijuana patients' claims that marijuana provides relief from their debilitating condition, MAPS submitted an Investigational New Drug application for marijuana to the Food and Drug Administration (FDA). This was the first step in a complicated bureaucratic process to gain approval for the study. MAPS outlined a protocol for a "placebo-controlled, triple-blind, randomized crossover pilot study of the safety and efficacy of five different potencies of smoked or vaporized marijuana in 50 veterans with chronic, treatment-resistant posttraumatic stress disorder."

The study would explore much more than whether marijuana makes PTSD sufferers feel better. By comparing the effectiveness of five strains with different ratios of tetrahydrocannabinol (THC) and cannabidiol (CBD), the study would help identify which strains work best for easing symptoms of PTSD. Additionally, by comparing the effects of smoked versus vaporized marijuana, the study would contribute to the available scientific data about which delivery systems are safest and most effective. The varying levels of potency in the protocol include a placebo (containing 0% THC and 0% CBD), as well as strains composed of 2%, 6%, and 12% THC; and a final strain composed of 6% THC and 6% CBD. The study will be conducted on an outpatient basis with individuals using up to two marijuana cigarettes a day (or the equivalent in a vaporized form) on a self-titration basis, where they decide the appropriate dose for symptom relief.

MAPS' efforts to start the study were initially delayed following the FDA's concerns that the marijuana used in the study would be diverted or sold for non-study uses. This concern was mainly due to the outpatient nature of the protocol. After hosting a teleconference with the FDA, MAPS successfully addressed the agency's concerns. MAPS submitted its revised protocol on March 15, 2011, and on April received word that the FDA was allowing the study to proceed.

Despite the fact that the FDA is the federal agency responsible for the development of new pharmaceutical drugs, MAPS then had to submit the protocol to the Department of Health and Human Services (HHS), to be reviewed by the National Institute on Drug Abuse (NIDA) and the Public Health Service (PHS), in order to secure marijuana for the study. The peculiar thing about this additional review process is that the vast majority of drugs being considered for clinical trials only need to pass the review process with the FDA. After they receive approval for their studies they are then able to obtain a private source of the drug and can begin the protocol. However, there is currently a monopoly on the source of marijuana for FDA approved studies that is administered by NIDA. This supply monopoly only exists for marijuana, and not for any other Schedule I controlled substances.

This additional review process allows the government to reject studies examining marijuana even after they have obtained clearance from the FDA. The reason for this is twofold. On one hand, the only proposals aside from those involving marijuana that must be submitted to

HHS are those attempting to secure government funding, which MAPS is not requesting. On the other hand, NIDA's mission statement explicitly states that they are dedicated to studying the adverse effects of drugs on society, which they claim precludes them from providing cannabis to studies into their possible beneficial uses. NIDA's monopoly therefore creates a situation that is inherently hostile to medical marijuana research.

Reviewers from NIDA and the PHS unanimously rejected MAPS' protocol on September 16, 2011. The reviewers based their rejection on what they claimed to be a lack of researcher expertise in dealing with PTSD, the difficulty of comparing the effectiveness of marijuana across subjects, assorted safety concerns that had already been addressed in MAPS' earlier negotiations with the FDA, and other details of study design. Many of these concerns are contradictory and unwarranted, especially given the fact that it is the FDA—not NIDA—that is charged with determining the effectiveness of proposed drug development studies. While NIDA and the PHS play a major role in determining which studies receive government funds, it's clear that their only purpose when it comes to marijuana research is to prevent it from happening.

MAPS has attempted to overcome the hurdle of NIDA's monopoly by appealing to the Drug Enforcement Administration (DEA) for a license to grow marijuana at a privately-operated farm. MAPS has advocated for Dr. Lyle Craker of the University of Massachusetts-Amherst to be granted an additional DEA license to cultivate marijuana for FDA approved studies for over a decade (see next article in this Bulletin). If this legal avenue eventually proves effective and MAPS finds a new source, Dr. Sisley will be able to proceed with the FDA-reviewed protocol.

It would be easy to get frustrated with the government's tactics, but my time working with MAPS has shown me that if any organization can overcome these obstacles, they can. MAPS is composed of some of the most dedicated individuals, both scientists and activists, that I have had the pleasure of encountering and I am proud to be a part of their legacy. I can say with confidence that MAPS' drive to improve the quality of life of those suffering from PTSD and other ailments is leading to a more just society, for it is only through the application of science that we can depoliticize this issue and find the most effective routes for treatment. •