

Obstruction of Medical Marijuana Research

Since 1968, all federally approved scientists have had to get their marijuana from the University of Mississippi, a source that researchers have complained is inadequate in quantity and quality. In 2001, Lyle Craker, a University of Massachusetts professor of plant biology, sought approval to cultivate marijuana for medical study. The agency turned him down, but a DEA administrative law judge ruled in February of 2007 that it "would be in the public interest" to allow Craker to grow the plants.

The 87-page ruling followed a nine-day hearing in which researchers recounted how the federal government rejected their requests for marijuana in FDA-approved research. Administrative law Judge Mary Ellen Bittner found that "an inadequate supply" of marijuana is available for research purposes. Her ruling is nonbinding.

Unlike in other areas of U.S. jurisprudence, the DEA administrator can ignore the ruling of the DEA's ALJ. Indeed, this happened in 1988, when the DEA's ALJ ruled that marijuana has medical value and should therefore be rescheduled from Schedule I to Schedule II under federal law. The DEA administrator refused to do so, and as a result, federal law still incorrectly asserts that marijuana is as dangerous as heroin and LSD -- and that cocaine and methamphetamine have more medicinal value than marijuana.

At present, only two cannabinoid drugs are licensed for U.S. sale: dronabinol (Marinol®) and nabilone (Cesamet®). Both are available in oral formulations only. While useful for some patients, these drugs have significant limitations. It is widely recognized that, as one recent review noted, "oral administration is probably the least satisfactory route for cannabis, owing to the sequestration of cannabinoids in fat from which there is slow and variable release into plasma. In addition, significant first-pass metabolism in the liver, which degrades THC, contributes to the variability of circulating concentrations of orally administered cannabinoids, which makes dose titration more difficult" (Baker et al., 2003). Peak concentrations of dronabinol and nabilone are typically not reached for at least an hour and can take up to four hours (Unimed, 2006; Valeant, 2006).

In addition, current research indicates that plant cannabinoids not contained in either approved drug may contribute significant benefit. For example, cannabidiol (CBD) has anti-emetic, analgesic, and anti-carcinogenic properties and also antagonizes certain undesirable effects of THC, including sedation and tachycardia (Russo and Guy, 2006).

Whole marijuana provides useful cannabinoids not presently available in pharmaceutical products. It can be taken orally, but in this form it suffers from the same pharmacokinetic drawbacks described above. Inhalation is widely preferred, producing far more rapid effects and allowing more accurate dose titration (Baker et al., 2003). Unfortunately, marijuana smoke contains tars and other unhealthful combustion byproducts, with some studies pointing to an increased risk of bronchitis and other respiratory ailments among marijuana smokers (Joy, Watson and Benson, 1999). However, lung cancer does not appear to be one of these risks. In contrast with tobacco, large-scale epidemiological studies have failed to detect elevated rates of tobacco-related cancers in long-term marijuana smokers who don't use tobacco (Sidney et al., 1997; Hashibe et al., 2006).

A natural marijuana extract in the form of a buccal spray, containing approximately equal proportions of THC and CBD, has been granted conditional approval in Canada and is

marketed under the brand name Sativex® for treatment of neuropathic pain in multiple sclerosis. Clinical trials have documented symptomatic relief, but the product's pharmacokinetics appear to be no better than those of oral dronabinol or nabilone, with peak concentrations achieved in 98 to 253 minutes. The product monograph approved by Health Canada notes, "This almost certainly reflects alimentary tract absorption of the proportion of the administered dose that is swallowed" -- a proportion which appears to be considerable (GW Pharma, 2006).

Because of concerns about smoking, the Institute of Medicine's 1999 review called for the development of "a nonsmoked, rapid-onset cannabinoid delivery system" (Joy, Watson and Benson, 1999). Vaporization provides such a delivery system for whole marijuana, taking advantage of the fact that cannabinoids vaporize at a temperature well below that at which marijuana burns. By heating the material to the proper temperature, vaporizers can provide the advantages of cannabinoid inhalation without the potentially harmful combustion products contained in smoke. A recent study of one such device confirmed this, concluding, "a safe and effective delivery system appears to be available to patients" (Hazekamp et al., 2006). However, further research on alternative routes of administration of rapidly available cannabinoid mixtures has been stymied by the lack of a reliable supply of pharmaceutical-grade cultivated cannabis in the U.S.

The current research climate for marijuana has created a significant chilling effect on researchers wanting to pursue FDA-approved clinical and basic research on the safety and efficacy of medical marijuana. We feel that it is appropriate for organized medicine to respond to the current legal limbo to help create a positive climate for increased research which would be best served by encouraging the federal government to authorize the Drug Enforcement Administration to license privately funded production facilities that meet all regulatory requirements to produce pharmaceutical-grade marijuana for use exclusively in federally approved research.