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REPORT 3 OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH (I-09) Use of Cannabis for Medicinal Purposes (Resolutions 910, I-08; 921, I-08; and 229, A-09) (Reference Committee K)

EXECUTIVE SUMMARY

<u>Objective</u>. This report: (1) provides a brief historical perspective on the use of cannabis as medicine; (2) examines the current federal and state-based legal envelope relevant to the medical use of cannabis; (3) provides a brief overview of our current understanding of the pharmacology and physiology of the endocannabinoid system; (4) reviews clinical trials on the relative safety and efficacy of smoked cannabis and botanical-based products; and (5) places this information in perspective with respect to the current drug regulatory framework.

Data Sources. English-language reports on studies using human subjects were selected from a PubMed search of the literature from 2000 to August 2009 using the MeSH terms "marijuana" "cannabis," and tetrahydrocannabinol," or "cannabinoids," in combination with "drug effects," "therapeutic use," "administration & dosage," "smoking," "metabolism," "physiology," "adverse effects," and "pharmacology." Additionally the terms "abuse/epidemiology," and "receptors, cannabinoid" in combination with "agonists," or "antagonists & inhibitors" as well as "endocannabinoids," in combination with "pharmacology," "physiology," or "metabolism" were used. Additional articles were identified by manual review of the references cited in these publications. Web sites of the Food and Drug Administration, Drug Enforcement Administration, National Institute on Drug Abuse, Marijuana Policy Project, ProCon.org, and the International Association for Cannabis as Medicine also were searched for relevant resources.

<u>Results</u>. The cannabis sativa plant contains more than 60 unique structurally related chemicals (phytocannabinoids). Thirteen states have enacted laws to remove state-level criminal penalties for possessing marijuana for qualifying patients, however the federal government refuses to recognize that the cannabis plant has an accepted medical benefit. Despite the public controversy, less than 20 small randomized controlled trials of short duration involving ~300 patients have been conducted over the last 35 years on smoked cannabis. Many others have been conducted on FDA-approved oral preparations of THC and synthetic analogues, and more recently on botanical extracts of cannabis. Federal court cases have upheld the privileges of doctor-patient discussions on the use of cannabis for medicinal purposes but also preserved the right of the federal government to prosecute patients using cannabis for medicinal purposes. Efforts to reschedule marijuana from Schedule I of the Controlled Substances Act have been unsuccessful to date. Disagreements persist about the long term consequences of marijuana use for medicinal purposes.

<u>Conclusions</u>. Results of short term controlled trials indicate that smoked cannabis reduces neuropathic pain, improves appetite and caloric intake especially in patients with reduced muscle mass, and may relieve spasticity and pain in patients with multiple sclerosis. However, the patchwork of state-based systems that have been established for "medical marijuana" is woefully inadequate in establishing even rudimentary safeguards that normally would be applied to the appropriate clinical use of psychoactive substances. The future of cannabinoid-based medicine lies in the rapidly evolving field of botanical drug substance development, as well as the design of molecules that target various aspects of the endocannabinoid system. To the extent that rescheduling marijuana out of Schedule I will benefit this effort, such a move can be supported.