



Marijuana Dispensaries and the Federal Government: Recommendations to the Obama Administration 2009: Part 2 **Andrea G. Barthwell, M.D.**

The Scientific Process

Crude Herbal Cannabis and Unstandardized Cannabis Preparations Do Not Meet the Standards of Modern Medicine.

The Institute of Medicine (IOM) has recognized that crude herbal cannabis has little future as a true medication:

Although marijuana smoked delivers THC and other cannabinoid to the body, it also delivers harmful substances, including most of those found in tobacco smoke. In addition, plants contain a variable mixture of biologically active compounds and cannot be expected to provide a precisely defined drug effect. For those reasons there is little future in smoked marijuana as a medically approved medication. If there is any future in cannabinoid drugs, it lies with agents of more certain, not less certain, composition.(50)

The IOM stressed that “the purpose of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug but rather to serve as a first step toward the development of non-smoked rapid-onset cannabinoid delivery systems.”(51)

The FDA agrees that crude herbal cannabis is not a medication.(52) The California Medical Association recently announced its intention to “re-examine the need for continued research on smoked herbal cannabis in light of recent research on its benefits and harm and the long-term prospect of smoked herbal cannabis as a medicine.”(53) The DEA also acknowledges the need for standardized product:

[H]erbal cannabis should comprise only the starting material from which a bona fide medical product is ultimately derived... [S]tandardizing herbal starting material represents only the first of many steps necessary to create a modern medicine that is safe and effective for use in specific medical conditions... [A] final medical product... must also be delivered in a dosage form that is consistent in composition and that allows the patient to obtain an identifiable and reliable amount of medication.(54)

Only Recently Has Technology Made Possible the Development of Modern Cannabis-derived and Cannabinoid Medications.

There are good reasons why the development of cannabis-derived medications has lagged far behind that of synthetic and naturally-derived opioids and other modern medications. Given that the active ingredients (morphine, codeine) of opium are water soluble, it was relatively simple in the 19th and early 20th centuries to isolate them and develop standardized and purified medications with the technologies that existed at that time.(55)

The story of cannabis is quite different. Cannabinoids (especially THC) are lipophilic (i.e., not water soluble) and unstable, making it difficult for early scientists to identify and isolate the active ingredients. Consequently, potentially therapeutic applications were limited to oral preparation of cannabis (tinctures and extracts),(56) which could not be adequately standardized. Patient response was variable and unpredictable. As more modern medicines became available, these unreliable extracts and tinctures fell out of favor with the medical profession.(57)

The modern era of cannabinoid research was in its infancy in 1964, when the primary psychoactive ingredient of cannabis, THC, was isolated and then synthesized.(58) Beginning in 1989, a robust body of cannabinoid research began to develop, following scientists' discovery of the human cannabinoid receptor system.(59) This delay in the development of modern cannabinoid and cannabis-derived medications has, therefore, been caused more by past technological limitations, than by governmental obstructionism. That development gap is now slowly closing, and there is no justification for affording a non-scientific acceleration, i.e., a "free pass," to herbal cannabis:

This evolution has followed the same principles as the evolution of drug therapy in general. The direction has been away from crude substances of variable composition, stability, and potency, toward the development of progressively more specific or selectively active pure compounds that permit more precise dosage and reduced risk of unwanted side effects.(60)

This is not to say that complex botanically-derived preparations cannot pass FDA muster. There is strong evidence that some properly tested and standardized plant preparations, including those derived from cannabis, may offer different -- and better -- pharmacological effects than a pure, synthesized cannabinoid alone.(61)

The FDA has recognized that there is burgeoning scientific and public interest in botanically-based products, and that modern technology makes it possible to develop medications of botanical origin. In order to guide the development of such products, the agency has set forth the criteria that must be met to achieve FDA approval.(62) While allowing some flexibility at the early stages of medication development, the guidance specifically states that, by the time of Phase 3 clinical studies,(63) the requirements for a botanical drug product are virtually the same as to those that apply to a new chemical entity (NCE). Botanical Raw Material (BRM), such as herbal cannabis, has not been formulated, incorporated into a specific dosage form, and tested through this demanding NCE process. The FDA guidelines make it quite clear that, even if crude herbal cannabis were moved to Schedule II, it could not thereby be marketed and distributed directly to patients.

The Administration Should Respect and Support the Proper Workings of the Scientific Process.

As a result of modern technologies, and as demonstrated by the receptor research mentioned above, there is significant interest within the scientific and medical communities in cannabinoid research. Scientists are moving as expeditiously as possible to bring new cannabinoid products to market. Time is required, however, for such research to be conducted in accordance with modern medical standards. In keeping with its commitment to science, this Administration should do nothing to discourage these efforts. As President Obama has stated:

Medical miracles do not happen simply by accident. They result from painstaking and costly research, from years of lonely trial and error, much of which never bears fruit, and from a government willing to support that work.(64)

The United States is, indeed, supporting such work in this area. For example, the FDA has allowed a cannabis-derived product to enter into advanced clinical trials in the U.S. For the past ten years, research has been underway in the United Kingdom by GW Pharmaceuticals to develop a range of prescription medications derived from the components of the cannabis plant. (65) GW cultivates particular strains of cannabis that have been bred to express specific ratios of cannabinoids. In order to maintain the consistency of the plants' chemical composition, they are grown by clones (cuttings) under highly-standardized and computer-controlled conditions in secure glasshouses. GW extracts the pharmacologically-active components of the plant, removes waxes and other unwanted constituents, and formulates the resulting botanical drug substance into a final dosage form of specified composition, which is characterized by various standard chromatographic techniques.

The company's lead product, Sativex®, is an oromucosal (inside of the mouth) spray composed primarily of THC and CBD. It is believed that this combination has distinct and important pharmacological activity. The product has already been approved in Canada for neuropathic pain in multiple sclerosis and for cancer pain. The DEA has licensed the importer(66) and the research sites.

A number of other companies, including Alexa Pharmaceuticals, Inc. (THC aerosol product); Aphios (naturally-derived THC product); and Insys Therapeutics, Inc., are also developing cannabinoid products in the U.S.(67) All of these research programs are moving through the conventional domestic regulatory process.(68) None is attempting to distribute crude herbal cannabis, or non-standardized botanical preparations, to pharmacies and patients.(69) These research programs indicate that cannabis-derived medications can, and therefore should, be developed within the parameters of modern regulatory oversight. Allowing a proliferation of cannabis dispensaries would undermine these efforts to bring properly tested medications to market, a result at odds with this Administration's position that its policies should be based on sound science.(70)

Developing properly standardized and tested cannabis-derived or cannabinoid medications is not an easy matter; it requires patience, perseverance, and a commitment of substantial resources. But numerous medical tragedies(71) have proven that shortcuts to the FDA process do a disservice to patient safety and well-being. The FDA drug approval process is not perfect, as demonstrated by recent news about previously-unknown dangers of marketed medications, such as Vioxx®.(72) The lesson of these experiences, however, is not that we should do less testing, or lower our current standards, for prescription medicines. Indeed, those incidents have led to demands for greater oversight by the FDA and, recently, for the establishment of an independent institute to examine the comparative safety and effectiveness of medications.(73)

The FDA Has Limited Power to Protect Patients Who Seek Medical Treatment and Advice From Cannabis Dispensaries.

The FDA has limited jurisdiction to address the dangers posed by cannabis dispensaries. The provisions of the FDCA govern only products that have been introduced into interstate commerce. Therefore, it can be argued that the activities of intra-state cannabis dispensary operations are beyond the reach of the FDA. Ironically, the FDA has greater power over dietary supplements (which have generally passed through interstate commerce) and over health food stores than it does over cannabis dispensaries and their operators.(74) Indeed, the manufacturers of herbs and other dietary supplements (and the retail establishments that sell them) are prohibited by federal law from making claims regarding the product's medical usefulness or specific health effects.(75) Cannabis dispensaries, however, do give out advice, and provide books and pamphlets, containing such medical claims.(76)

The DEA, therefore, plays a critical part in protecting patients from dangerous, ineffective, and federally unapproved cannabis products. The CSA, and therefore the DEA's authority, extends to products containing controlled substances and activities that may affect interstate commerce, even if the specific products have been manufactured and distributed solely within the state.(77) If this Administration ties the DEA's hands with regard to dispensaries, patients will lose altogether any avenue of federal protection.

States Laws and Regulatory Bodies Should Enhance, Rather Than Undermine, the Protections Provided by the FDA System.

In cases other than medical marijuana, the FDA and DEA are able to rely to a large extent on state regulatory and law enforcement systems to support and augment the federal structures. States have generally accepted this responsibility, enacting their own food and drug laws to fill the gap in the FDA's jurisdiction. These state laws are, for the most part, modeled after the federal FDCA. In California, for example, the Sherman Food, Drug, and Cosmetic Law ("Sherman Law") establishes rigorous scientific standards that must be met before a new drug may be marketed for medical use. The Sherman Law states that a new drug generally may not be sold, delivered, or given away unless a new drug application has been filed with, and approved by, the state or federal government.(78)

State regulatory boards and agencies similarly enhance the effectiveness of the FDA and DEA. State boards of medicine, nursing, pharmacy, etc., supervise the education, training, and practices of all health care providers who examine or advise patients, or dispense or distribute medications. Health care providers who do not adhere to accepted standards of medical practice may incur sanctions from these boards, as well as risk potential civil liability for inappropriate prescribing or other conduct falling below the standard of care.(79) Health care facilities are monitored and licensed by state departments of health services. State tort systems allow patients who have suffered injury from a medication to seek damages from the manufacturer, even if that medication has been FDA-approved.(80) These state mechanisms, when they operate effectively, provide patients with additional or greater avenues of redress and protection and, thereby, complement federal food and drug provisions.

By contrast, when states utilize their food and drug laws (or enact other state legislation) for the purpose of circumventing the FDCA, patient health and safety is jeopardized. In many ways, the current cannabis controversy parallels the Laetrile controversy of the 1970s. At that time, Laetrile (amygdalin) was vigorously promoted as a cancer treatment and preventative. Despite efforts by its supporters to characterize it as a dietary supplement ("Vitamin B17"), the FDA determined that Laetrile was a new drug (since it was intended for medical use) and was subject to premarketing approval.(81) Since it had not been proven safe and effective for medical use, the FDCA precluded Laetrile's shipment in interstate commerce. Desperate cancer patients, spurred on by anecdotal reports of efficacy, contended that they had a right to use Laetrile, despite evidence of cyanide toxicity. Laetrile advocates claimed that the FDA, the American Medical Association, the American Cancer Society, the pharmaceutical companies, and others were conspiring against Laetrile.(82) This political pressure, rather than scientific evidence, caused twenty-seven state legislatures to pass laws allowing the sale and use of Laetrile within their borders. These state laws had little effect, since it was not feasible to manufacture Laetrile within each state. "Proponents hoped, however, that if enough states legalized its use within the states, Congress would change the federal law as well."(83) Ultimately, the National Cancer Institute conducted clinical testing and determined that Laetrile was not effective as a cancer treatment.(84) The lesson of Laetrile is that state legislation should only be used to enhance, rather than undermine, the protections of the federal regulatory system.

The same is true with regard to controlled substances. Many states have adopted the Uniform Controlled Substances Act,(85) the provisions of which parallel those of the federal CSA. States can serve as an early warning system, and have the flexibility to respond more quickly to abuses of controlled substances -- or of uncontrolled substances with abuse potential -- within their borders.(86) For example, as an added layer of protection, states may require that individuals who conduct research into controlled substances must be independently inspected, licensed, and/or approved by state agencies, in addition to obtaining DEA registrations.(87) States may enact prescription monitoring programs to track physicians who prescribe controlled substances, in order to identify and stop inappropriate prescribing practices by physicians, as well as “doctor shopping” by patients (obtaining prescriptions from multiple doctors simultaneously).(88) States also have greater flexibility in their scheduling actions. If a state believes that a new substance has abuse potential and poses a threat to patient safety or public health, the state need not wait on the DEA; it may schedule that substance more restrictively, or prohibit its sale and use altogether.

Cannabis Dispensaries Are Not Subject to State Laws and Regulations Applicable to Entities Operating in the Health Care Area.

Cannabis dispensaries starkly conflict with this robust state system of patient-oriented controls. “Pot docs,” for cash payments of several hundred dollars, provide recommendations to patients (including minors), with whom they have virtually no physician-patient relationship, to enable them to use cannabis for a wide variety of medical conditions.(89) Patients purchase cannabis from dispensaries with which they have only a retailer-consumer relationship. Dispensary personnel need not be licensed as health care providers, nor are they required to follow proper sterile techniques to protect against on-site bacterial(90) or other contamination of the herbal material, although it is intended for consumption directly by patients.(91) Despite their lack of training and accreditation, such personnel freely offer medical information and advice to patients (92) about the panoply of cannabis products, including extracts, capsules, tablets, and various types of edibles. Some of these products can reach THC concentrations as high as 80%, which could produce significant side effects, especially in seriously ill patients or those who have not used cannabis before.(93)

At best, cannabis dispensaries are regulated at the local level.(94) Where they are permitted by local legislation (as in San Francisco),(95) such dispensaries are not regulated as if they were health care facilities (e.g., clinics or pharmacies) answerable to the state department of health services. Nor are the employees who provide direct patient service (e.g., distributing medical marijuana or medical advice) subject to the scope of practice restrictions and requirements supervised by the state boards of pharmacy, nursing, and medicine. Rather, dispensaries are regulated as if they were retail establishments, subject only to the Building, Planning, Housing, Police, Fire, and Health codes of the local jurisdiction.(96)

Cannabis and Cannabis-Derived Products Should be Governed by the Quality Control and Other Testing Procedures Applicable to All Modern Medications.

Gradually, even some cannabis dispensaries have begun to voice concern that these unregulated distribution practices may be placing patients in danger. One operator has acknowledged that, if cannabis “is going to become an accepted mainstream medicine,” there must be quality assurance and dosage information:

[A] dog walks in the grow room, and wags its tail—anything can be coming off that dog’s tail. It’s gross. Fertilizers with E. coli. Compost ... that they don’t make right, anaerobic tea that has elevated levels of E. coli and salmonella. It has to come. There’s no way that this is sustainable.

All it takes is one story of immune-compromised people dying from *Aspergillus* infection.(97)

This operator has affiliated with an informal laboratory, and envisions a testing program using such instruments as a gas chromatograph and mass spectrometer.(98) He also notes, however, that “It’s expensive to test every single thing that comes through the door—that’s the price you pay with a decentralized supply system... five pounds coming from here and two from there.”(99) It is far from certain whether other dispensaries would voluntarily join such an effort.

These rudimentary laboratory-testing efforts merely confirm the importance of adhering to the existing body of technological tools and methodologies mandated by state and federal regulatory agencies. There is no need to “recreate the wheel” for cannabis or cannabis-derived preparations. Drug manufacturers are already required to institute extensive testing procedures to ensure that their products are quality-controlled during manufacture, and that their formulations and dosage forms are standardized and reproducible. Testing procedures must be validated, instruments must be calibrated, equipment operators must be appropriately educated and trained, careful records must be kept, and practices must be sterile. Finished medical products must be analyzed for batch-to-batch consistency, and any degradants and minor contaminants must be identified and strictly limited.

Should a system of cannabis-testing laboratories ultimately develop at all, it is hard to imagine that it would be allowed to operate at a different or inferior level to the current U.S. medication-development system. If cannabis dispensaries are allowed to proliferate across the country, our current regulatory system, to which the American Medical Association and all other major U.S. medical associations give their unwavering support, may be seriously undermined.

If there were only a single state with a few dispensaries, the risk might not be as significant. At present, however, 13 states have laws decriminalizing the use of cannabis for medical purposes, and bills are pending in many more states.(100) If such cultivation and distribution activities are deemed to be beyond the reach of the DEA, dispensaries are likely to emerge all over the country. (101)

The United States’ International Obligations

Good Science Should Also Guide Decisions Implementing Our Obligations Under International Drug Control Treaties.

President Obama has announced his intention to trust science and research when designing our international, as well as domestic, policies. Sound science should inform and guide this Administration as it implements our international responsibilities in the field of drug control policy. The U.S. -- and thereby the Department of Justice -- has an obligation under our international drug control treaties to control strictly the manufacture and distribution of controlled substances, including the cultivation and distribution of cannabis, within our borders.

In particular, if the U.S. permits the cultivation of cannabis plants for medical use, it must apply the same provisions as are imposed for the cultivation of the opium poppy for medical use. This rigorous system of controls must be maintained by a single government agency. States, therefore, cannot have sole jurisdiction over the proliferation of cannabis dispensaries.

The United States is a signatory to the Single Convention on Narcotic Drugs 1961 (“Single Convention”).(102) This treaty was intended to ensure that the production and use of narcotic

substances are limited exclusively to bona fide medical and scientific purposes.(103) Accordingly, the Single Convention requires a party to impose strict controls, not merely on international trade, but also on domestic manufacture, distribution, import, export, and possession of botanically-derived controlled substances (such as coca, opium, and cannabis).

The phrase “medical and scientific purposes” has a clear meaning. The treaty was promulgated at a time when governments around the world were developing regulatory procedures to ensure the quality and safety of medical products.(104) Crude narcotic plant material was not considered suitable for direct medical use. For example, under the treaty, opium smoking was not an accepted method for delivering the therapeutically useful components contained within the herbal material.(105)

The Single Convention recognized that different countries may have different regulatory systems. (106) However, the treaty expected that each party would in good faith adhere to modern scientific standards: that is, employ conventional regulatory standards when determining whether, when, and which, narcotic substances and products could be made available for medical use. Nowhere in the treaty is there any suggestion that a Party may allow a diluted or informal medical system solely for a specific controlled substance such as cannabis.

In response to the activities of medical cannabis proponents, the International Narcotics Control Board (INCB)(107) stressed that a party may not allow cannabis to be cultivated, manufactured, and used for medical purposes unless such products have satisfied the rigorous regulatory standards that apply to other medical products. Such use must be supported by objective scientific data from properly-conducted research studies, and must otherwise accord with principles of modern medicine.(108)

The Single Convention places particularly severe restrictions on the cultivation of cannabis, opium, and coca bush. Article 23 requires that, if a party permits(109) cultivation of opium poppies within its borders, the Party must establish and maintain a national Agency to carry out the Party’s obligations. Articles 26 and 28 apply those requirements to the cultivation of the coca bush and the cannabis plant, respectively. Article 23 requires that only nationally-licensed cultivators, whose license specifically identifies the precise extent and location of the land that they are authorized to cultivate, may grow such narcotic plants.(110) They must deliver their total crops to the Agency, and only the national Agency may deal with such crops. The Agency must have the exclusive right of importing, exporting, wholesale trading, and maintaining stocks.(111)

The National Institute on Drug Abuse (NIDA) serves as the U.S. national Agency under the Single Convention.(112) Under the auspices of NIDA, the U.S. maintains a domestic cultivation facility, in which research-grade cannabis is cultivated by the National Center for Natural Products Research at the University of Mississippi under contract with NIDA.(113) This cannabis is supplied to investigators who have research protocols that have been approved by the FDA and by an expert committee of the Public Health Service, and who have obtained research registrations from the DEA.(114) As of April 2004, the University of Mississippi, with the approval of NIDA and the PHS committee,(115) had provided cannabis to more than 17 clinical and preclinical studies funded by the Center of Medicinal Cannabis Research (CMCR) at the University of California San Diego.(116)

If, in the future, cannabis-derived medications were to be developed and approved for marketing, it would not be necessary for the cannabis cultivation (production of starting materials) to take place in the United States. The herbal material, or the Botanical Drug Substance (extracts) could be imported into the U.S. for further formulation. For over 85 years, it has been the policy of the U. S. not to cultivate or produce narcotic raw material (NRM), such as opium, poppy straw, and

concentrate of poppy straw (CPS).(117) By long-standing international policy, the U.S. is a country that imports and consumes, rather than one that produces and supplies, NRM.(118) The U.S. relies on a specific list of countries authorized to import NRM into the U.S. in order to meet the legitimate medical needs of the U.S.(119) This list is deliberately kept very short, in order to prevent a proliferation of NRM-producing countries.

Furthermore, the treaty imposes additional controls on all manufacture and distribution of cannabis-derived and other controlled substances. Such activities must be conducted by federally-licensed and regulated entities that are producing standardized products for medical or research purposes.(120) Therefore, were the U.S. to permit dispensaries in various states across the country to distribute(121) or cultivate cannabis for medical use, the U.S. would be in violation of these unmistakably clear treaty obligations. The INCB has confirmed this position:

The control measures applied in California for the cultivation, production and use of cannabis do not meet the control standards set in the 1961 Convention to prevent diversion of narcotic drugs for illicit use. Such standards require, inter alia, the control of cultivation and production of cannabis by a national cannabis agency, and detailed record keeping and reporting on the activities with cannabis, including reporting to INCB.(122)

The Controlled Substances Act Was Enacted in Part to Fulfill Our Obligations Under the Single Convention, and the Proliferation of Cannabis Dispensaries Cannot be Left Solely to State Control.

The federal CSA was enacted, in part, to fulfill the United States' obligations under the Single Convention.(123) The CSA and its implementing regulations have two prongs. They are designed:

- 1) to ensure that there is a sufficient supply of controlled substances for legitimate medical, scientific, research, and industrial purposes; and
- 2) to prohibit, deter, and punish the sale and use of controlled substances to illegal purposes.

These goals parallel those of the Single Convention: to ensure that narcotic and other psychoactive substances are manufactured, traded, and used only for legitimate (i.e., evidence-based) medical and scientific purposes. If the DEA were prohibited from shuttering cannabis dispensaries and seizing the materials purveyed therein, the U.S. would have failed to comply with its international responsibilities. If the U.S. does not abide by its treaty obligations, other countries will be unlikely to adhere to theirs. As in other arenas, the U.S. should seek to be a leader with respect to modern medical science and its responsibilities under international agreements.

The CSA achieves its purposes by:

- 1) establishing a process (scheduling) through which scientific and other data may be used to ensure appropriate levels of control of abuseable substances, and the adequate availability of medications containing them;(124) and

2) creating a “closed” system, in which every importer, exporter, manufacturer, distributor, dispenser, and researcher handling a controlled substance must meet strict licensing, recordkeeping, and security requirements, which are consistent with those required by the Single Convention.

Cannabis dispensaries operate entirely outside of this system of controls. It is hard to see the logic or merit of any position that would relieve cannabis dispensaries from federal oversight, despite the fact that cannabis is a Schedule I substance, while requiring manufacturers and distributors of Schedule II substances to secure DEA registrations, adhere to quotas, keep accurate records, and institute strict security measures. The DEA has both the power⁽¹²⁵⁾ and the obligation to curb the proliferation of cannabis dispensaries. It cannot abdicate this responsibility in the name of deferring to states’ rights.⁽¹²⁶⁾

Under the Single Convention, the United States must in good faith strive to prevent the non-medical sale and use of controlled substances. A decision by the Administration to prevent the DEA from intervening in cannabis dispensaries, if they are “authorized” under state law, will effectively prevent the agency from enforcing the CSA against cannabis retail storefronts that are merely subterfuges for non-medical distribution of cannabis.

State and local law enforcement do not alone possess adequate resources to stem the proliferation of dispensaries that distribute cannabis for non-medical use. Moreover, local law enforcement needs the assistance of the DEA in combating these operations. These entities do not have access to the highly efficient law enforcement tools that the DEA has at its disposal. For example, local law enforcement cannot utilize federal asset forfeiture laws to deter landlords from permitting cannabis distribution activities to take place on their property.⁽¹²⁷⁾ Indeed, attempting to require the DEA selectively to halt only non-medical distribution centers will require the DEA to dissipate its limited resources in a futile line-drawing exercise.

The process of identifying cannabis dispensaries that distribute cannabis for non-medical use would be extremely onerous for a federal agency. In order to fulfill its unquestioned obligation to enforce the CSA’s and Single Convention’s prohibitions against non-medical distribution, the DEA would be required to examine the records of dispensaries to make the following assessments: the true non-profit nature of the entity; the means by which physician recommendations are verified; the bona fides of members and the relative labor, monetary, or other resource contributions of those members to the non-profit enterprise; the source of the cannabis; and whether it can be determined to have been cultivated in all cases by legitimate members, etc.⁽¹²⁸⁾

Moreover, the DEA’s resource-intensive struggle to distinguish between legitimate (under state law) and unlawful (under state law) dispensaries would be compounded by the fact that, increasingly, cannabis dispensaries have delivery services.⁽¹²⁹⁾ Such delivery services would make it even more difficult for the DEA to track and evaluate cannabis distribution activities for compliance with state law.

Even for local jurisdictions, detailed state guidelines, such as those issued by the California Attorney General, are difficult enough to interpret and enforce. To require the DEA to take a hands-off approach to any dispensary that may be operating in accordance with such state guidelines would effectively ban the DEA from any significant cannabis interdiction, leading to a free-for-all of cannabis dispensaries across the state and, potentially, across the nation. As a result, cannabis would become readily available for any use—both medical and recreational.⁽¹³⁰⁾

Conclusion

For the reasons stated above, the Obama Administration must take a measured approach in addressing marijuana dispensaries, maintaining the commitment to enforcing the CSA that the Department of Justice has recently reiterated. This commitment must be met even in states that authorize “medical” use of marijuana, and especially where illegal distributors attempt to use state medical marijuana laws as a pretext. We recognize that the Department of Justice and the DEA have limited resources, and those resources must be spent wisely. The United States, however, also has both domestic and international responsibilities to protect the health and safety of patients and to promote the responsible development of modern medications. A fixed Administration ruling against DEA intervention into the operations of cannabis dispensaries would allow informal, quasi-medical networks to spring up across the nation, thereby putting at risk the critical protections so carefully crafted under the national food and drug legislation of the 20th and 21st centuries.

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52. In 2001, in rejecting a petition for the rescheduling of marijuana , the FDA stressed:

The agency cannot conclude that marijuana has an acceptable level of safety without assurance of a consistent and predictable potency and without proof that the substance is free of contamination. If marijuana is to be investigated more widely for medical use, information and data regarding the chemistry, manufacturing and specifications of marijuana must be developed.

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53. California Medical Association, ON-CALL document #1315 (Jan. 2009). <http://www.cmanet.org>.

54. DEA, Lyle E. Craker; Denial of Application, 74 Fed. Reg. 2101, 2105 (Jan. 14, 2009), citing Letter from Alice P. Mead, GW Pharmaceuticals, PLC, to Christine V. Beato, Acting Asst. Sec. for Health, HHS (Apr. 12, 2005).

55. As technologies advanced, synthetic medicines appeared, necessitating the promulgation of a subsequent treaty, the Psychotropic Convention of 1971.

56. Cannabis was generally not smoked at that time for medical purposes.

57. “Unlike cannabis, the medicinal and recreational forms of opium were clearly distinct. Had medical technology been advanced enough at that time to allow cannabinoids to be identified, formulated, and delivered, the “medical marijuana” movement would probably not have occurred. As with the opium poppy, prescription cannabinoid medications and crude herbal cannabis would have been used in very different venues.” McCarberg, WH and Barkin RL, “The Future of Cannabinoids as Analgesic Agents: A Pharmacologic, Pharmacokinetic, and Pharmacodynamic Overview,” (2007) *American Journal of Therapeutics* 14(5); 475-483,476 (emphasis added).

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60. Kalant, H, "Smoked Marijuana as Medicine: Not Much Future," *Clinical Pharmacology & Therapeutics*, (April 2008) 83:4; 517-519, 517.

61. McPartland JM, Russo EB, "Cannabis and Cannabis Extracts: Greater Than the sum of Their Parts?" *Journal of Cannabis Therapeutics*. 2001; 1(3-4):103-132.

62. FDA, Guidance for Industry: Botanical Drug Products, 2004, <http://www.fda.gov/cder/guidance/4592fnl.pdf> (hereinafter Botanical Guidance) at p. 34. ("A botanical product submitted for marketing approval as a drug will be treated like any other new drug under development... [P]revious human experience may be insufficient to demonstrate the safety of a botanical product, especially when it is indicated for chronic therapy.")

63. This is the last stage of human research before the submission of a marketing application or NDA.

64. Montopoli, B., "Obama Announces Stem Cell Decision," *CBS News Political Hotsheet* (Mar. 9, 2009) (President Obama remarks in full) at p. 2.

65. GW Pharmaceuticals, Research & Development / Cannabis Cultivation. http://www.gwpharm.com/research_cultivation.asp.

66. The original registration was originally granted in 2006, 71 Fed. Reg. 64298 (Nov. 1, 2006), and was recently renewed. 73 Fed. Reg. 9589 (Feb. 21, 2008). Clinical trials began in November 2007. <http://www.gwpharm.com/states.asp>.

67. Such efforts are not confined to the U.S. ; see, e.g., Echo Pharmaceuticals (the Netherlands) (Namisol, a naturally-derived THC in sublingual tablet form). The U.S. (through NIDA) has also provided research-grade cannabis to a number of researchers whose studies have been funded by grants from the Center of Medicinal Cannabis Research, which is based at the University of California San Diego. The results of a number of these studies have been published (www.cmcr.ucsd.edu/geninfo/marijuana.htm) and respond to the IOM's statements that such clinical trials serve "as a first step toward the development of nonsmoked rapid-onset cannabinoid delivery systems." *Marijuana and Medicine*, supra, at p. 11.

68. Indeed, even the staunchest herbal cannabis advocates are recognizing the need to develop standardized cannabis pharmaceutical products with "innovative formulations." <http://www.phytiva.com>.

69. The path of Cannasat is instructive. Cannasat, the only firm in Canada devoted to the development of cannabinoid medications, initially extolled the benefits of herbal cannabis plant

material. Recently, it sold off its ownership interests in the cannabis cultivation program operated under contract from Health Canada and is developing synthetic cannabinoids with “proprietary formulations and drug delivery technologies.” <http://www.cannasat.com/news-5.html>. <http://www.cannasat.com/>.

70. The Institute of Medicine has described the many financial and other challenges that would be faced by a developer of legitimate cannabis-derived pharmaceutical products, even if a parallel, “informal” system of dispensaries did not exist. To allow such dispensaries would increase these disincentives and potentially prevent the U.S. from responding to the IOM’s call for the development of rapid-onset, alternative delivery systems for cannabis- or cannabinoid-based products. *Marijuana and Medicine*, supra, at pp. 193-219.

71. For example, the Elixir Sulfanilamide disaster led to the enactment of the 1938 Food, Drug & Cosmetic Act (FDCA), June 25, 1938, c.675, 52 Stat. 1040, which required, among other things, that new drugs be tested for safety before marketing. The thalidomide tragedy in Europe led to the passage of the Drug Amendments of 1962, Pub. L. 87-781, sec. 1, Oct. 10, 1962, 76 Stat. 780 (also known as the Kefauver-Harris Amendments), which required that products be proved to be both safe and effective before marketing.

72. <http://www.fda.gov/cder/drug/infopage/COX2/default.htm>. “FDA Estimates Vioxx Caused 27,785 Deaths,” (Nov. 4, 2004). http://www.consumeraffairs.com/news04/vioxx_estimates.html.

73. Walker, EP, “Stimulus Bill Gives \$1.1 Billion for Comparative Effectiveness Research,” *MedPage Today* (Feb. 19, 2009).

74. Dietary supplements are already subject to a lower standard of regulatory scrutiny because they are presumed to be less dangerous than prescription medications and because they are not intended -- and cannot be labeled or advertised as -- for use in diagnosing, mitigating, treating, or curing disease. See, the Dietary Supplement Health and Education Act of 1994 (DSHEA), 21 U.S.C. §321(ff). Dietary supplements are orally ingested. FDA Botanical Guidance at p. 3.

75. See The Dietary Supplement Health and Education Act of 1994 (DSHEA), Pub. L. 103-417. <http://www.fda.gov/opacom/laws/DSHEA.html>. Whether a product is a drug under the FDCA turns on its “intended use.” “Intended use,” in turn, is created by claims made by or on behalf of a manufacturer or distributor of the item to prospective purchasers, such as in advertising, labeling, or oral statements. 21 U.S.C. §321(g)(1)(B); Botanical Guidance at p. 2. Dietary supplement manufacturers, distributors, or retailers cannot make specific health claims. See, e.g., *U.S. v. 24 Bottles “Sterling Vinegar and Honey Aged in Wood Cider Blended With Finest Honey Contents 1 Pint Product of Sterling Cider Col, Inc., Sterling, Mass.”* 338 F.2d 157 (2nd Cir. 1964); *Kordel v. U.S.*, 335 U.S. 345 (1948).

76. See, e.g., “California Law Enforcement Investigating ‘Pot Docs’” (July 8, 2008). [http://www.officer.com/web/online/Top-News-Stories/California-Law-Enforcement-Investigating-Pot-Docs/1\\$31450](http://www.officer.com/web/online/Top-News-Stories/California-Law-Enforcement-Investigating-Pot-Docs/1$31450).

77. *Gonzales v. Raich*, 545 U.S. 1 (2005).

78. Calif. Health & Safety Code §111550.

79. If physicians prescribe unapproved medications (those that are not approved by the state or

federal regulatory agency), and a patient suffers harm as a result, the physician's professional liability policy may not cover a claim for damages. See, Educating Voices "The Potential Medical Liability for Physicians Recommending Marijuana as a Medicine," (white paper). http://www.educatingvoices.org/EVI_WhitePaper1.pdf.

80. Wyeth v. Levine, 555 U.S. ____ (Mar. 4, 2009).

81. 42 Fed. Reg. 39,768-39,795 (1977).

82. Bone, M., MD, "Laetrile Drug Never Proved to be Effective Cancer Treatment," The Palm Beach Post (Mar. 20, 2008).

83. Wilson, B., MD, "The Rise and Fall of Laetrile." <http://www.quackwatch.org/01QuackeryRelatedTopics/Cancer/laetrile.html>.

84. Moertel CG et al., "A Clinical Trial of Amygdalin (Laetrile) in the Treatment of Human Cancer," New England Journal of Medicine 1982; 306(4):201-6. Nevertheless, even at present, companies continue to promote and sell Laetrile as a cancer treatment through internet web sites. See, e.g., FDA Talk Paper, "FDA Takes Action Against Firms Marketing Unapproved Drugs," (Sept. 6, 2000). <http://www.fda.gov/bbs/topics/ANSWERS/ANS01032.html>.

85. See, National Conference of Commissioners on Uniform State Laws. http://www.nccusl.org/nccusl/uniformact_summaries/uniformacts-s-ucsa90.asp. Calif. Health & Safety Code §§11000-11651.

86. For example, Salvia divinorum (whose active constituent is salvinorin A) is an herb that is increasingly used by the public for its hallucinogenic effects. Salvia is not currently controlled under the CSA, although the DEA is observing it closely. As of November 2008, thirteen states had enacted legislation placing regulatory controls on Salvia divinorum and/or salvinorin A; a number of those states placed the substances in schedule I of state law. Proposed legislation is pending in a number of other states. DEA, "Drugs and Chemicals of Concern," Nov. 2008. http://www.deadiversion.usdoj.gov/drugs_concern/index.html.

87. The Research Advisory Panel (RAP) of the California Attorney General's office must approve all Schedule I and II research projects and protocols. Calif. Health & Safety Code §§11480-81. <http://caag.state.ca.us/research>.

88. DEA, State Prescription Drug Monitoring Programs. http://www.deadiversion.usdoj.gov/faq/rx_monitor.htm. When controlled substances are at issue, the federal government also has authority to regulate directly some aspects of a physician's medical practice. Under the CSA, physicians who prescribe or dispense controlled substances must hold a registration from the DEA, and such controlled substances must be prescribed for a legitimate medical purpose and in the course of regular professional practice. 21 C.F.R. §1306.04(a); U.S. v. Moore, 423 U.S. 122, 137, 140-42 (1975). Although states bear the primary responsibility for preventing and punishing the diversion of (prescription) controlled drugs by health care providers, the DEA in egregious cases may investigate and revoke the registration of (and even criminally prosecute) a physician or other health care provider who facilitates and/or promotes drug abuse and addiction.

89. See, e.g., "California Law Enforcement Investigating 'Pot Docs'" (July 8, 2008). <http://www>.

officer.com/web/online/Top-News-Stories/California-Law-Enforcement-Investigating-Pot-Docs/1\$31450. The Medical Board of California has promulgated guidelines for physicians who recommend cannabis; however, there has been very limited enforcement. http://www.medbd.ca.gov/Medical_Marijuana.html. Physicians who recommend cannabis can avoid the need for a DEA registration if they do not prescribe other controlled substances.

90. Salmonella and E. coli are common bacterial contaminants that can be transmitted to botanical material through improper handling techniques.

91. San Francisco regulations state that dispensary operators must require employees only to “wash hands” and “use sanitary utensils” when handling cannabis, rather than use sterile gloves and instruments. Sec. 3312(b)(3).

92. As one dispensary advertises: “We are also experienced and knowledgeable about the various medications and how they work for various ailments, so we can steer you toward an answer, not just another dead end.” <http://greendragoncoop.com/default.htm?gclid=CKWtgr6wj5kCFRBbagodxhFTZg>. http://www.mlive.com/news/flint/index.ssf/2009/03/group_to_offer_marijuana_advic.html. <http://www.sanfranciscocannabisclubs.com/directory/san-francisco-green-door.htm> (patients can expect to deal with “knowledgeable” staff members).

93. Downs, D., “The Manhattan Project of Marijuana,” East Bay Express (Mar. 4, 2009) <http://www.eastbayexpress.com/ebx/PrintFriendly?oid=936926>. Hereinafter “Manhattan Project.”

94. Many cities have no regulations and, indeed, have issued bans or moratoria. <http://www.scribd.com/doc/294869/Medical-Marijuana-moratorium-map>.

95. Medical Cannabis Act revisions, Official San Francisco Website. <http://www.sfgov.org/site/uploadedfiles/bdsupvrs/ordinances09/o0025-09.pdf>.

96. Cannabis is a highly abuseable substance and, if determined to have an accepted medical use in treatment in the U.S. , would remain subject to the closed system of distribution required by the CSA. State regulation does not fulfill this requirement.

97. Manhattan Project, supra.

98. Of course, this “laboratory” is a far cry from currently-acceptable scientific standards (“looks like a bachelor pad with a locked room in the back”). Id.

99. Id.

100. For example, bills are pending in Illinois, Minnesota, New Hampshire, and New York, among others to decriminalize cannabis for medical use. <http://www.mpp.org/legislation>.

101. For example, a bill is currently pending in the Rhode Island legislature to amend the existing “medical marijuana” law to authorize cannabis dispensaries. This bill has gained more force following Attorney General Eric Holder’s remarks, although it failed in the state House of Representatives last year. Members of the House have stated that the Attorney General’s comments have caused them to view the proposal “much more favorably” than last year.

Needham, C., "Bill Would License Dispensaries to Sell Medical Marijuana" (Mar. 5, 2009). http://www.projo.com/news/content/MARIJUANA_BILL_03-05-09_UNDHM3N_v17.37894c1.html.

102. Single Convention on Narcotic Drugs, March 30, 1961, 18 U.S.T. 1407.

103. Single Convention, preamble, Art. 4c.

104. The need for the practice of medicine to be "evidence-based" had become well-established, particularly in the Western world. For several decades, scientists had been conducting randomized, placebo-controlled clinical trials to investigate the safety and efficacy of investigational medical products. Chow, S. and Liu, J., *Design and Analysis of Clinical Trials*, p. 4 (1998). Then, as now, the results of such clinical trials formed the basis both of governmental regulators' marketing approvals and physicians' prescribing practices. See Guyatt, G. et al., "Evidence Based Medicine: Principles for Applying the Users' Guides to Patient Care," 284 *Journal of the American Medical Association* 1290 (Sept. 13, 2000).

105. Cannabis and cannabis resin were placed in Schedule IV, the treaty's most restrictive schedule, whereas oral cannabis preparations, i.e., tinctures and extracts, were placed in Schedule I, along with most other narcotic drugs. The Single Convention's schedule structure does not parallel that of the Controlled Substances Act, in which Schedule I is the most restrictive.

106. See Secretary General of the United Nations, *Commentary on the Single Convention on Narcotic Drugs, 1961, (1973)*, para. 12, p. 111 ("legitimate" existing systems of indigenous medicine may be taken into account) (hereafter *Commentary*).

107. The INCB is the United Nations organ created by the Single Convention to implement, and monitor compliance with, the Convention. See *Single Convention*, arts. 5, 9-15, 19-20.

108. INCB, *Report 2002*, at p. 21 (2003).

109. The treaty imposes other, very specific restrictions on the cultivation of cannabis, opium, and coca. Article 22 requires a Party to prohibit cultivation, if the Party concludes in good faith that the "prevailing conditions" in the country make such prohibition the most suitable measure of protecting the public health and safety. Furthermore, a Party that prohibits such cultivation must "take appropriate measures" to seize and destroy any plants that are illegally cultivated, except for small quantities that the Party itself may need for scientific or research purposes.

110. The *Commentary* also indicates that, under the Single Convention, all licensed cultivators "should to the greatest extent possible, be located in the same part of the country, and be contiguous, in order to facilitate more effective control." *Commentary* at p. 280. This provision would not permit the establishment of cannabis cultivation sites in numerous locations all over the U.S.

111. Preparations of cannabis, such as pharmaceutical-grade extracts and tinctures, are exempt from the government monopoly on wholesale distribution. *Single Convention*, art. 23, para. 1(e). The treaty also does not extend the government's exclusive rights to "medicinal opium and opium preparations." *Id.* at art. 23, para. 2(e). "Medicinal opium" is a form of opium powder to which lactose has been added to reduce the morphine content to the standard of about 10 percent." *Commentary* at p. 21-22. In other words, the term "referred to a product which had not only been extracted from the opium poppy but had also undergone several further processes ... to prepare

it for use in other drugs and to obtain a specific and standardized content of morphine, its primary active ingredient.” DEA, “Lyle E. Craker; Denial of Application,” 74 Fed. Reg. 2101, 2104 (Jan. 14, 2009) at p. 2116. “[T]here were recognized standards for the substance’s manufacture and composition and ... the drug had an accepted medical use in humans.” Id. By contrast, “there are no recognized standards with respect to herbal marijuana.” Id. Therefore, cannabis, even if intended for medical use, d

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