UNITED STATES DEPARTMENT OF JUSTICE
Drug Enforcement Administration

In the Matter of **Lyle E. Craker, Ph.D.**	Docket No. 05-16

OPINION AND RECOMMENDED RULING, FINDINGS OF FACT, CONCLUSIONS OF LAW, AND DECISION OF THE ADMINISTRATIVE LAW JUDGE

MARY ELLEN BITTNER, ADMINISTRATIVE LAW JUDGE

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Dated: February 12, 2007

TABLE OF CONTENTS

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INTRODUCTION

This proceeding is an adjudication pursuant to the Administrative Procedure Act, 5 U.S.C. § 551 et seq., to determine whether an application for registration with the Drug Enforcement Administration (DEA) as a bulk manufacturer of the Schedule I substance marijuana should be denied. Without this registration, Respondent Lyle E. Craker, Ph.D., of Amherst, Massachusetts, will be unable lawfully to cultivate marijuana in order to supply it to analytical, preclinical, and clinical researchers.

On December 10, 2004, the Deputy Assistant Administrator, Office of Diversion Control, DEA, issued an Order to Show Cause to Respondent, proposing to deny his application to be registered as a bulk manufacturer of marijuana on grounds that such registration would not be consistent with the public interest as that term is used in 21 U.S.C. § 823(a) and with the United States' obligations under the Single Convention on Narcotic Drugs, 1961.[1] More specifically, the Order to Show Cause alleged, in substance, that:

1. On June 28, 2001, Respondent submitted an application to the DEA as a dosage form manufacturer of marijuana. The DEA did not process this application but returned it to Respondent and requested that he resubmit the application as a bulk manufacturer of marijuana and that he submit answers to questions about his plans for such manufacture. Respondent prepared answers

[1] Single Convention on Narcotic Drugs, March 30, 1961, 18 U.S.T. 1407, 520 U.N.T.S. 204 (as amended March 25, 1972, 26 U.S.T. 1439, 976 U.N.T.S. 3) [hereinafter Single Convention].

to these questions and resubmitted his application on August 28, 2002. Respondent noted in his answers, *inter alia*, that he, through the University of Massachusetts, Department of Plant and Soil Science, proposed to cultivate marijuana in order to supply it to analytical, preclinical, and clinical researchers.

2. On September 9, 2003, Mahmoud A. ElSohly, Ph.D., Research Professor and Director of the National Institutes of Health Marijuana Project, submitted comments on and objections to Respondent's application pursuant to 21 C.F.R. § 1301.33.

3. The National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health (NIH), which is in turn a component within the Public Health Service (PHS) of the United States Department of Health and Human Services (HHS), oversees the cultivation, production, and distribution of research-grade marijuana on behalf of the United States Government. NIDA fulfills this obligation through a contract it administers currently with the University of Mississippi, National Center for Natural Products Research (National Center), which is the only entity currently registered with the DEA to manufacture (cultivate) marijuana for the purpose of supplying the United States with research-grade marijuana. Based on the NIDA contract, the National Center then supplies the marijuana it cultivates to the Research Triangle Institute (RTI). RTI, which is registered with the DEA to manufacture marijuana, has a subcontract with the University of Mississippi to process the National Center's marijuana into cigarettes. RTI then distributes the marijuana cigarettes to DEA-registered researchers who utilize the marijuana for experimental clinical use. All of the foregoing activities take place under the supervision of NIDA.

4. NIH, through NIDA, permits marijuana to be distributed to DEA-registered researchers only pursuant to the arrangement it has with the National Center and RTI. NIH's policy requires that to be eligible to receive marijuana through this arrangement, researchers must submit their research protocols for review and approval by a PHS interdisciplinary review process. The PHS

reviews the scientific quality of the proposed researcher's study, the quality of the researcher's peer-review process, and the objectives of the proposed research.

5. In accordance with the federal Food, Drug, and Cosmetic Act (FDCA), any researcher who seeks to develop a new drug for medical use must submit an Investigational New Drug (IND) application to the Food and Drug Administration (FDA) of HHS. To obtain approval for marketing under the FDCA, the researcher is required to conduct both clinical and preclinical studies to demonstrate the safety and effectiveness of the new drug. Prior to the new drug's introduction in humans, the researcher must demonstrate that it will be safe for use in initial, small-scale studies by presenting the appropriate preclinical data to the FDA. A Phase I study is the initial introduction of the investigational new drug into humans. It is conducted in a small number of healthy volunteers to characterize the drug's metabolic and pharmacologic action in humans, and the adverse effects associated with increasing doses of the drug. Phase II studies evaluate the drug's effectiveness in patients who have the disease or condition the product is intended to treat. Phase III studies evaluate the drug's safety, effectiveness, and dosage. These clinical trials are controlled and uncontrolled studies conducted in hundreds or thousands of patients. All INDs, whether they are controlled substances or not, must comply with these FDA procedures.

6. In addition, any researcher who seeks to conduct research in which humans will be supplied with marijuana must comply with the PHS review process as described above. If the researcher satisfies the criteria established by HHS, the researcher will be eligible to receive marijuana at cost through NIDA. NIDA makes the marijuana available to the researchers through its contract with the National Center.

7. If the University of Massachusetts' application to obtain a DEA registration to cultivate marijuana were granted, the Multidisciplinary Association for Psychedelic Studies (MAPS) would subsidize the University of Massachusetts' cultivation of marijuana. MAPS maintains that a second

manufacturing registration is needed because the researchers who obtain marijuana from the National Center through NIDA do not receive the quantity or quality of marijuana that they require. DEA personnel have contacted these researchers to determine whether MAPS' claims are substantiated. Based upon the contacts, the DEA determined that the researchers are obtaining from the National Center marijuana of sufficient quantity and quality to meet all of their legitimate and authorized research needs in a timely manner.

8. MAPS also maintains that NIDA is limited to supplying marijuana for research purposes and cannot supply marijuana on a prescription basis. MAPS further contends that this limitation effectively prohibits a sponsor (such as a pharmaceutical company) from expending the necessary large amounts of funds to conduct drug development studies resulting in a marijuana prescription product. MAPS contends that this problem will be resolved by granting Respondent's application to manufacture marijuana. MAPS, through these arguments, has not shown that granting Respondent's application would be consistent with the public interest based upon the following:

   a. Current marijuana research has not progressed to Phase II of the clinical trials because current research must utilize smoked marijuana, which ultimately cannot be the permitted delivery system for any potential marijuana medication due to the deleterious effects and the difficulty in monitoring the efficacy of smoked marijuana.

   b. In accordance with the Single Convention, the federal Government must limit marijuana available for clinical research to one source. Based upon this mandate of the Single Convention, HHS, through NIDA, submits a contract to open bidding every five years to determine which one enterprise will be allowed to cultivate marijuana. Since this HHS policy is consistent with the Single Convention, DEA has no authority to overturn it. Moreover, the DEA agrees with HHS' policy inasmuch as it accords with DEA's interpretation of the Single Convention.

9. In compliance with and consistent with 21 U.S.C. § 823(a) and the Single Convention, and consistent with marijuana's status as a Schedule I controlled

substance, DEA must limit the number of producers of research-grade marijuana to that which can provide an adequate and uninterrupted supply under adequately competitive conditions. For the past thirty-six years, the University of Mississippi has provided such supply under the foregoing criteria, and there is no indication that this registrant will fail to do so throughout the duration of its current registration. While the University of Massachusetts is free to compete with the University of Mississippi to obtain the next NIDA contract to produce research-grade marijuana for the United States, there is no basis under § 823(a) to add another producer.

10. MAPS maintains that Schedule I DEA research registrants are not required to undergo additional scrutiny of their proposals by the PHS except for Schedule I research registrants who perform clinical research with marijuana. MAPS, through this argument, has not shown that granting Respondent's application would be consistent with the public interest because:

    a. The latter policy is one that is mandated by HHS and, therefore, DEA has no statutory authority to overturn it.

    b. Marijuana is the most heavily abused of all Schedule I controlled substances, and limiting the supply of marijuana under these circumstances is reasonable.

    c. The system has not unduly limited clinical research with marijuana. Since 2000, there have been or are eleven approved clinical trials utilizing smoked marijuana, three approved clinical sub-studies on side effects of marijuana, and four approved preclinical trials in laboratory and animal modes. Current registered marijuana researchers administer marijuana to almost 500 human subjects. Research with other Schedule I controlled substances is not as extensive as it is with marijuana at this time.

Respondent, through counsel, timely filed a request for a hearing on the issues raised by the Order to Show Cause. Following prehearing procedures, a hearing was held in Arlington, Virginia, on August 22 through 26 and December 12 through 14 and 16, 2005. At the hearing, both parties called witnesses to testify and introduced documentary evidence. After the hearing, both parties filed proposed findings of fact, conclusions of

law, and argument. All of the evidence and posthearing submissions have been considered, and to the extent the parties' proposed findings of fact have been adopted, they are substantively incorporated into those set forth below.

ISSUE

Whether a preponderance of the evidence establishes that granting Respondent's application for registration as a manufacturer of the Schedule I controlled substance marijuana would be in the public interest, as that term is used in 21 U.S.C. § 823(a).

RELEVANT TREATY, STATUTORY, AND REGULATORY PROVISIONS

I. The Controlled Substances Act

The Controlled Substances Act provides, at 21 U.S.C. § 823(a), that the Deputy Administrator is to register an applicant to manufacture a Schedule I controlled substance if she determines that such registration is consistent with the public interest and with the United States' obligations under international treaties, and that in determining the public interest, the Deputy Administrator is to consider the following factors:

(1) maintenance of effective controls against diversion of particular controlled substances and any controlled substance in Schedule I or II compounded therefrom into other than legitimate medical, scientific, research, or industrial channels, by limiting the importation and bulk manufacture of such controlled substances to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes;
(2) compliance with applicable state and local law;
(3) promotion of technical advances in the art of manufacturing these substances and the development of new substances;
(4) prior conviction record of applicant under federal and state laws relating to the manufacture, distribution, or dispensing of such substances;
(5) past experience in the manufacture of controlled substances, and the existence in the establishment of effective control against diversion; and
(6) such other factors as may be relevant to and consistent with the public health and safety.

It should be noted here that Respondent has the affirmative burden of showing that his registration would be in the public interest.[2] It should also be noted that the Deputy Administrator may give each of the factors listed in 21 U.S.C. § 823(a) the weight she deems appropriate in determining whether a registration should be revoked or

[2] 21 C.F.R. § 1301.44(a).

an application for registration denied.[3]

The Controlled Substances Act further provides, at 21 U.S.C. § 823(f), that:

> Registration applications by practitioners wishing to conduct research with controlled substances in Schedule I shall be referred to the Secretary [of Health and Human Services], who shall determine the qualifications and competency of each practitioner requesting registration, as well as the merits of the research protocol. The Secretary, in determining the merits of each research protocol, shall consult with the Attorney General as to effective procedures to adequately control diversion of such controlled substances from legitimate medical or scientific use. Registration for the purpose of bona fide research with controlled substances in Schedule I by a practitioner deemed qualified by the Secretary may be denied by the Attorney General only on a ground specified in [21 U.S.C. § 824]. Article 7 of the Convention on Psychotropic Substances shall not be construed to prohibit, or impose additional restrictions upon, research involving drugs or other substances scheduled under the convention which is conducted in conformity with this subsection and other applicable provisions of this subchapter.

II. The Single Convention on Narcotic Drugs

The Single Convention on Narcotic Drugs, 1961 (Single Convention) is an international treaty adopted in 1961 and amended in 1972 and to which the United States is signatory.[4] Article 4 of the Single Convention requires signatory parties to take such legislative and administrative measures as may be necessary:

a) To give effect to and carry out the provisions of this Convention within their own territories;
b) To cooperate with other States in the execution of the provisions of this Convention; and
c) Subject to the provisions of this Convention, to limit exclusively to medical and scientific purposes the production, manufacture, export, import, distribution of, trade in, use, and possession of drugs.[5]

Article 23 of the Single Convention specifies a system of controls on the cultivation of opium poppies;[6] Article 28 applies those same controls to the cultivation of marijuana.[7] In combination, Articles 23 and 28 require a signatory country that permits the cultivation of marijuana to establish a government agency[8] to oversee such

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[3] *See Henry J. Schwarz, Jr., M.D.*, 54 Fed. Reg. 16,422 (1989).
[4] Single Convention, *supra* note 1.
[5] Single Convention, art. 4, para. 1.
[6] Single Convention, art. 23.
[7] Single Convention, art. 28.
[8] The Single Convention requires that there be only one such agency if the signatory's constitution permits it. Single Convention, art. 23, para. 3.

cultivation. This agency is responsible for designating the areas and plots of land on which cultivation may occur, licensing cultivators, and specifying in the licenses the extent of the land on which cultivation is permitted.[9] Paragraph 2 of Article 23 also requires that cultivators of the opium poppy deliver their total crops of opium to the government agency, that the agency purchase and take physical possession of the crops, and that the agency have the exclusive right of importing, exporting, wholesale trading, and maintaining stocks other than those held by manufacturers of opium alkaloids, medicinal opium, or opium preparations.[10] Paragraph 2(e) adds that signatories need not extend this exclusive right to medicinal opium and opium preparations.[11]

Article 1, paragraph (1)(o) of the Single Convention defines "medicinal opium" as "opium which has undergone the processes necessary to adapt it for medicinal use."[12] Article 1, paragraph (1)(x) defines "stocks" as the amount of drugs held in a country or territory and intended for:

i) Consumption in the country or territory for medical and scientific purposes,
ii) Utilization in the country or territory for the manufacture of drugs and other substances, or
iii) Export;

but does not include the amount of drugs held in the country or territory:

iv) By retail pharmacists or other authorized retail distributors and by institutions or qualified persons in the duly authorized exercise of therapeutic or scientific functions, or
v) As "special stocks."[13]

The Commentary to the Single Convention notes that "special stocks" and likewise retail "stocks" (i.e. opium held in stock by retail pharmacists or other authorized retail distributors and by institutions or qualified persons in the duly authorized exercise of therapeutic or scientific functions) are both excluded from the scope of the obligatory Government monopoly. Such special stocks and retail stocks are not "stocks" within the meaning of the Single Convention.[14]

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[9] Single Convention, art. 23, para. 2(a)-(c).
[10] Single Convention, art. 23, para. 2(d)-(e).
[11] Single Convention, art. 23, para. 2(e).
[12] Single Convention, art. 1, para. 1(o).
[13] Single Convention, art. 1, para. 1(x).
[14] Commentary on the Single Convention on Narcotic Drugs, 1961 (prepared by the

III. Regulations Implementing the Controlled Substances Act

The DEA's regulations specify, at 21 C.F.R. § 1301.33(b), that "[i]n order to provide adequate competition, the [Deputy] Administrator shall not be required to limit the number of manufacturers in any basic class to a number less than that consistent with maintenance of effective controls against diversion solely because a smaller number is capable of producing an adequate and uninterrupted supply."

IV. Other Relevant DEA Statements

By notice published in the *Federal Register* on September 18, 1975, the DEA adopted a policy that it would no longer grant import registrations for Schedule I and II controlled substances if the applicant was seeking the registration in order to import only in the event of an emergency involving the domestic supply of raw material.[15] The policy therefore stated that all applicants for registration would be required to demonstrate that the requirements of 21 U.S.C. §§ 958(a) and 823(a) and of what is now 21 C.F.R. §§ 1301.34(b), (c), (d), (e), and (f) are satisfied. This same policy has been applied or considered in final orders on applications for registration to manufacture as well as applications for registration to import.[16]

FINDINGS OF FACT

I. Background

A. About Respondent

Marijuana is a Schedule I controlled substance, which means that it has a high potential for abuse, it has no currently accepted medical use in treatment in the United States, and there is a lack of accepted safety for its use under medical supervision.[17] As more fully discussed below, research with Schedule I substances is permitted, provided the Secretary of Health and Human Services deems the researcher qualified and has approved the research protocol, and provided that the researcher is registered with the

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Secretary-General), art. 23, para. 2(e), commentary 4.

[15] Registration of Importers; Statement of Policy and Interpretation, 40 Fed. Reg. 43,745 (1975).

[16] *Performance Construction, Inc.*, 67 Fed. Reg. 9,993 (2002); *Houba, Inc.*, 69 Fed. Reg. 8,696 (2004). I note, however, that these applications were not the subject of adjudicative proceedings.

[17] 21 U.S.C. § 812(b)(1).

DEA to conduct the research.[18]

There are more than 480 substances in marijuana, and about sixty-six of them are cannabinoids, chemical compounds that contain twenty-one carbons and in nature exist only in the marijuana plant. The major cannabinoid is tetrahydrocannabinol (THC), which exerts most of marijuana's pharmacological activities. There are several THCs, but the one usually referenced by the term tetrahydrocannabinol is delta-9-THC, and references to THC herein are to delta-9-THC unless otherwise indicated. Other cannabinoids mentioned in this proceeding are cannabichromene, a cannabinoid that does not have psychological activities but does have anti-inflammatory and antimicrobial activity, and cannabidiol, a variety-specific cannabinoid that is usually present in comparatively small amounts in the varieties of marijuana that have a high THC content.

Marijuana is a dioceous plant, i.e., it has both female and male plants; when plants are grown from seed, approximately half the resulting plants will be male and the other half will be female. Sensimilla is the buds from female plants that are not fertilized by male plants and thus do not produce seeds; the brach, the leafy structure that protects the ovaries, has the highest THC content in the plant, and the brach from sensimilla plants can have THC potencies of fifteen to twenty-four percent or more.

1. About the Risk of Diversion of Marijuana

As noted above, marijuana has a high risk of abuse, as indicated by its placement in Schedule I under the Controlled Substances Act. In a January 2005 report, NIDA stated that:

> Currently, marijuana is the most commonly used illicit drug in the [United States], with recent estimates from SAMHSA [the Substance Abuse and Mental Health Services Administration] of 14.6 million users in the past month and particularly heavy use occurring in adolescent populations (over 20 percent of all high school seniors). Approximately 2.4 million people use marijuana for the first time every year and [two thirds] of them are between 12 and 17 years of age. In addition, of the 3.5 million people who met criteria for past-year cannabis abuse or dependence in 2001, more than [two thirds] were between the ages of 12 and 25 years. An estimated 852,000 individuals reported marijuana as the specific substance for which they received their last or current treatment among persons who received treatments in the past year and approximately [one half] of those individuals were 25 years old or younger.

[18] 21 U.S.C. § 823(f).

> Sufficient research has been carried out to confirm that the use of cannabis can produce serious physical and psychological consequences. The consequences of cannabis use may be due to the acute effects of the drug or due to the chronic exposure that may ultimately produce abuse or dependence. The use of a large amount in a short period of time may induce hallucinations, delirium, and other perceptual manifestations compatible with a psychotic episode. Chronic users of cannabis may experience difficulty in stopping or controlling drug use, develop tolerance to the subjective and cardiovascular effects, and eventually present withdrawal symptoms after sudden discontinuation of use.[19]

Nora Volkow, M.D., Director of NIDA, gave a statement on medical marijuana to the Criminal Justice, Drug Policy, and Human Resources Subcommittee of the Government Reform Committee of the House of Representatives on April 1, 2004. Dr. Volkow stated that marijuana is the most commonly used illicit drug in the United States, and that according to the 2002 National Survey on Drug Use and Health, more than ninety-five million Americans twelve years of age and older had tried marijuana at least once.

Dr. Volkow stated that when an individual is intoxicated by marijuana, short-term memory, attention, judgment, and other cognitive functions are disrupted, and that marijuana has also been shown to impair coordination and balance and could increase heart rate. Dr. Volkow further stated that longer-lasting cognitive defects have been reported in heavy marijuana users, although these defects had been reversible after sustained abstinence, and that a marijuana withdrawal syndrome characterized by increased anxiety, drug craving, sleep difficulties, and decreased appetite can last from several days to a week following abstinence. According to Dr. Volkow, this withdrawal is similar to that experienced after abstaining from nicotine. Dr. Volkow further stated that early marijuana use is associated with an increased likelihood of lifelong drug problems, and that one study found that adolescents who had been prenatally exposed to marijuana performed worse on tasks requiring visual memory, analysis, and integration.

Eric Voth, M.D., F.A.C.P.,[20] is board-certified in internal medicine and

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[19] National Institute on Drug Abuse (NIDA), *Report on the Rare Diseases Research Activities at the National Institutes of Health FY 2003* (last reviewed Jan. 28, 2005) <http://rarediseases.info.nih.gov/html/reports/fy2003/nida.html>; Government exhibit 43, p. 9.

[20] F.A.C.P. is the abbreviation for Fellow of the American College of Physicians; the College bestows these fellowships upon physicians in recognition of academic and

specializes in that field of medicine and in addiction medicine. According to an article Dr. Voth co-authored that was published in 2004,[21] "[a]lthough most cannabis use is intermittent and time-limited, an estimated 10-20% of American and Australian adolescents who smoke cannabis become dependent on one or more drugs."[22] The article further cites a finding in a report by a working party of the Royal College of Psychiatrists and Royal College of Physicians which states that surveys in North America indicate that five to ten percent of persons who have used cannabis more than once become dependent.

Dr. Voth testified that the incidence of marijuana use drops "quite a lot"[23] after the age of twenty-five years, but that the incidence of physical dependence among fourteen- or fifteen-year-olds is at least five percent. Dr. Voth further testified that the earlier a person starts using a drug, the more likely he/she is to become addicted to it, and that individuals who do not use any intoxicant until they are at least twenty-one years old are much less likely to become addicted.

Dr. Voth testified that the short-term effects of ingesting THC include a sense of intoxication, along with concomitant behaviors and mood changes such as lack of coordination, concentration, and short-term memory involvement, increased heart rate, and sedation; and that dysphoria, panic attacks, and psychotic episodes can also occur. Dr. Voth testified that long-term effects of THC include habituation or dependence, worsening of memory disorders and ability to concentrate, and increasing risk of psychotic and other psychiatric disorders. Dr. Voth further testified, however, that it is impossible to ingest a lethal dose of THC because it does not affect the brain stem. Dr. Voth also testified that smoking marijuana with higher concentrations of THC increases the risk that adverse effects will occur. Dr. Voth testified that smoking marijuana causes harshness for the throat and lungs, unrelated to the concentration of THC in the material.

Dr. Voth testified that there are carcinogens in marijuana, but that there is a

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professional accomplishments.

[21] Richard H. Schwartz, M.D. & Eric A. Voth, M.D., *The use and toxicity of cannabis in teenagers*, *in* 21 RECENT ADVANCES IN PAEDIATRICS 131-144 (Royal Society of Medicine Press Ltd. 2004); Government exhibit 41.

[22] *Id.* at 139 (citing Wayne Hall & Nadia Solowij, *Adverse effects of cannabis*, 352 THE LANCET 1611-1616 (1998)); Government exhibit 41.

conflict in the literature as to whether smoking marijuana can cause cancer. Dr. Voth noted that marijuana does not contain nicotine, which definitely causes lung cancer.

Dr. Voth testified that he is opposed to the legalization of marijuana, i.e., the legality of leaf marijuana for recreational smoking, and that he considers medical marijuana an excuse for legalization and therefore opposes it. Dr. Voth further testified, however, that he supports research on the medical use of cannabinoids and other components of marijuana, and that there is evidence on the potential medical use of various cannabinoids.

According to the National Drug Intelligence Center's National Drug Threat Assessment 2005, published in February 2005, marijuana production within the United States was expected to increase, and:

> An increased supply of marijuana likely will result in increased exposure to the drug and consequently more new users, since initiates to drug use are more likely to start with a drug that is as readily available and easily obtainable as marijuana. Indeed, reporting from some areas has suggested that marijuana is easier for youths to obtain than alcohol or cigarettes. Among established users, particularly among older teens and young adults, the general softening of attitudes regarding the risks associated with and the disapproval of marijuana use, combined with increased availability of the drug, should presage a rise in consumption.[24]

A 2004 article[25] explored the risk of becoming dependent on marijuana within twenty-four months after the first use of the drug and found, among other things, that there was a strong association between beginning marijuana use at eleven to thirteen years of age and dependence, that educational attainment was inversely associated with the risk of becoming dependent soon after onset of use, and that there was more risk of dependence among those who had used three or more drugs (including tobacco and alcohol) prior to their first use of marijuana and among those with a family income of less than $20,000.

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[23] Transcript p. 1,947.

[24] National Drug Intelligence Center, *National Drug Threat Assessment 2005* (Feb. 2005) <http://www.usdoj.gov/ndic/pubs11/12620/marijuana.htm>; Government exhibit 45, p. 31.

[25] Chuan-Yu Chen, Megan S. O'Brien, & James C. Anthony, *Who becomes cannabis dependent soon after onset of use? Epidemiological evidence from the United States 2000-2001*, 79 DRUG AND ALCOHOL DEPENDENCE 11-22 (2005); Government exhibit 49.

2. The 1995 Petition to Reschedule Marijuana

In 2001 the DEA denied the March 10, 1995 petition of a Jon Gettman to initiate rulemaking proceedings to reschedule marijuana.[26] In a letter to Mr. Gettman published in the notice, the then-Administrator stated that before initiating rulemaking proceedings to reschedule a controlled substance, the Administrator must gather requisite data and request from the Secretary of the Department of Health and Human Services a scientific and medical evaluation and a recommendation as to whether the substance should be rescheduled. The then-Administrator noted that pursuant to 21 U.S.C. § 811(c), in determining whether to reschedule a controlled substance the Administrator must consider:

> (1) its actual or relative potential for abuse;
> (2) scientific evidence of its pharmacological effect, if known;
> (3) the state of current scientific knowledge regarding it;
> (4) its history and current pattern of abuse;
> (5) the scope, duration, and significance of abuse;
> (6) what, if any, risk there is to the public health;
> (7) its psychic or physiological dependence liability; and
> (8) whether it is an immediate precursor of a substance already controlled.

The then-Administrator found that the Assistant Secretary for the Department of Health and Human Services had determined that marijuana has a high potential for abuse, an assessment also supported by data the DEA had gathered, and that this finding alone required denying the petition; that the petitioner had not asserted that marijuana has a currently accepted medical use in the United States or was safe to use under medical supervision; and that the Department of Health and Human Services evaluation had reaffirmed the finding that marijuana did not have such a current accepted medical use and was not safe for use under medical supervision. The then-Administrator further stated in the letter that:

> when it comes to a drug that is currently listed in Schedule I, if it is undisputed that such drug has no currently accepted medical use in treatment in the United States and a lack of accepted safety for use under medical supervision, and it is further undisputed that the drug has at least some potential for abuse sufficient to warrant control under the [Controlled Substances Act], the drug must remain in Schedule I.[27]

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[26] Notice of Denial of Petition, 66 Fed. Reg. 20,038 (2001).
[27] Notice of Denial of Petition, 66 Fed. Reg. at 20,039.

3. The Institute of Medicine Report on Use of Marijuana for Medical Purposes

Barbara Roberts, Ph.D., senior policy analyst in the White House Office of National Drug Control Policy (ONDCP) from 1994 until 2003, and Acting Associate Deputy Director for ONDCP's Office of Demand Reduction from mid-2002 to August 2003, testified that the use of marijuana for medical purposes became a very controversial issue while she was working at ONDCP and that she consequently recommended that the Institute of Medicine[28] be asked to study the question. In 1999 the Institute of Medicine issued its report, *Marijuana and Medicine: Assessing the Science Base*.[29] Dr. Roberts characterized the response to the report as "muted,"[30] and testified that she did not think that very much was done with it.

The report specifically recommended that:

> (1) Research should continue into the physiological effects of synthetic and plant-derived cannabinoids and the natural function of cannabinoids found in the body. Because different cannabinoids appear to have different effects, cannabinoid research should include, but not be restricted to, effects attributable to THC alone.[31]
> (2) Clinical trials of cannabinoid drugs for symptom management should be conducted with the goal of developing rapid-onset, reliable, and safe delivery systems.[32]
> (3) Psychological effects of cannabinoids such as anxiety reduction and sedation, which can influence medical benefits, should be evaluated in clinical trials.[33]

The report also stated, among other things, that:

> Marijuana delivered in a novel way that avoids smoking would overcome some, but not all, of the regulatory concerns. Vaporization devices that permit inhalation of plant cannabinoids without the carcinogenic combustion products found in smoke are under development by several groups; such devices would also require

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[28] Dr. Roberts testified that the Institute of Medicine is a component of the National Academy of Sciences and is a "medical think tank" funded by Congress where leading researchers and scientists study specific issues. Transcript p. 287.
[29] JANET E. JOY, STANLEY J. WATSON, JR., & JOHN A. BENSON, JR., DIVISION OF NEUROSCIENCE AND BEHAVIORAL HEALTH, INSTITUTE OF MEDICINE, MARIJUANA AND MEDICINE: ASSESSING THE SCIENCE BASE (National Academy Press 1999); Respondent exhibit 1.
[30] Transcript p. 294.
[31] JOY, *supra* note 29, at 3.
[32] *Id.* at 4.
[33] *Id.* at 5.

regulatory review by the FDA.[34]

Dr. Roberts testified that she did not recall any effort within ONDCP to recommend to NIDA that it pursue the idea of vaporized marijuana, and that although there was discussion within the ONDCP about the report, no formal action was taken.

The report further stated, "The effects of cannabinoids on the systems studied are generally modest, and in most cases there are more effective medications,"[35] and that the Controlled Substances Act poses substantial regulatory obstacles to marketing marijuana, but that if marijuana receives FDA approval as a drug it would probably be rescheduled.

In addition, the report stated that:

> Defined substances such as purified cannabinoid compounds are preferable to plant products which are variable and of uncertain composition. Use of defined cannabinoids permits a more precise evaluation of their effects, whether in combination or alone. Medications that can maximize the desired effects of cannabinoids and minimize the undesirable effects can very likely be identified.[36]

Dr. Roberts testified that in her view, the Institute of Medicine report "in a way really provided a blueprint for us, . . . to investigate this and to put it to rest,"[37] and that "[a] tremendous amount of money is spent in the prohibition of [marijuana's] use for medicinal purposes, but certainly I think having the research to resolve this issue would be most beneficial."[38] Dr. Roberts further testified that she thought that having an alternative to NIDA as a supplier of marijuana for research would encourage competition and that she saw no reason not to have such an alternative source.

B. The Agencies and Organizations Involved in Marijuana Cultivation and Research

1. About the National Institute on Drug Abuse

The National Institute on Drug Abuse (NIDA) is one of the National Institutes of Health (NIH), which in turn is an agency of the Public Health Service within the Office of the Secretary of the Department of Health and Human Services. Dr. Roberts, the former Acting Associate Director of ONDCP, testified that NIDA is one of fifty-five agencies that have responsibilities for substance abuse issues and that report to the

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[34] *Id.* at 216.
[35] *Id.* at 3.
[36] *Id.* at 4.
[37] Transcript p. 302.

ONDCP, and that NIDA conducts about eighty-five percent of the world's research in substance abuse policy.

Steven Gust, Ph.D., Special Assistant to the Director of NIDA, testified that NIDA is one of the twenty-seven or so institutes and centers that comprise NIH, and that NIDA's mission is "to support research on the causes, consequences, prevention, and treatment of drug abuse and drug addiction."[39] NIDA also administers the National Drug Supply Program, which provides controlled substances and their precursors to researchers. The National Drug Supply Program supplies some other Schedule I substances to researchers and there are additional suppliers of some Schedule I substances, but NIDA is the sole supplier of marijuana for research purposes. Dr. Gust testified that it is not NIDA's mission to study medicinal uses of marijuana or to advocate for such research.

2. About the University of Mississippi's Work with Marijuana

The University of Mississippi is a state university with a campus in Oxford, Mississippi. Since about 1968 the University of Mississippi has held a registration from the DEA or its predecessor agency to cultivate marijuana for government use and research activities, and at some point the National Center for Natural Products (National Center), part of the Research Institute of Pharmaceutical Sciences of the University of Mississippi's School of Pharmacy, obtained a registration to manufacture marijuana specifically for NIDA. The National Center holds another manufacturer registration that permits it to develop pharmaceutical preparations from the marijuana plant.

The National Center is currently the only DEA-registered cultivator of marijuana. The University of Mississippi has a competitively-renewed contract with NIDA pursuant to which the National Center supplies marijuana to researchers for studies ranging from chemical research to preclinical toxicology in animals to clinical work on humans. As of the date of the hearing, the contract term was five years; prior to 1999 the contracts were awarded every three years. Starting with the 1999 contract, the University of Mississippi subcontracted to Research Triangle Institute (RTI) of North Carolina the manufacture of marijuana cigarettes, analysis of the THC and moisture content of the cigarettes, and

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[38] Transcript pp. 302-303.
[39] Transcript p. 1,625.

distribution of the cigarettes to researchers.[40]

The most recent contract covers the period March 16, 2005, through March 15, 2010, and requires the National Center to produce, store, analyze, and distribute marijuana as required by NIDA; to extract and isolate THC and other cannabinoids from marijuana for research purposes; to maintain specified stocks of high-THC content, low-THC content, and placebo cigarettes [g13/7]; and to maintain a specified stock of bulk marijuana. The contract also requires the National Center to analyze each month approximately 100 samples of confiscated marijuana provided by the DEA as a means of determining potency trends of illicit marijuana and of screening for herbicide contamination.

Dr. Gust testified that he oversees the NIDA contract with the University of Mississippi; that a program staff at NIDA develops a statement of work, outlining the work to be performed under the contract; that the statement of work is then put into a request for proposals and submitted to NIDA's Contract Procurement Office; and that that office announces the availability of the contract, receives applications for the contract, and reviews the applications. Dr. Gust further testified that NIDA does not inspect the National Center's growing operation or evaluate its security, nor does NIDA establish how much marijuana the National Center may grow other than pursuant to its contract with NIDA.

Dr. Gust testified that the DEA notified him of Respondent's instant application and that, consequently, he arranged for Respondent to be sent a notice of the availability of the most recent contract to cultivate marijuana. Dr. Gust testified that entities other than the University of Mississippi had bid on the contract to cultivate marijuana, but that he did not know who those entities were.

Mahmoud ElSohly, Ph.D., a research professor at the Research Institute of Pharmaceutical Sciences, is the Principal Investigator listed in the contract between the National Center and NIDA and as such, heads the National Center's work with marijuana. Dr. ElSohly testified that the National Center cannot ship marijuana or direct RTI to do so without obtaining approval from NIDA, that NIDA determines how much

[40] Prior to 1999 RTI manufactured the cigarettes, but pursuant to a separate contract with NIDA rather than as a subcontractor to the University of Mississippi.

marijuana the National Center will cultivate in a given year, and that in April 2004 the FDA inspected the University of Mississippi facility and did not find any deficiencies in its manufacturing practices.

Dr. ElSohly testified that the National Center analyzes marijuana samples from states as well as from the DEA, and that notwithstanding the contract provision requiring the National Center to analyze about 100 samples of confiscated marijuana per month, over the ten years preceding the hearing, the National Center had probably analyzed between 2,000 and 4,000 samples of marijuana per year. Dr. ElSohly testified that in about 1991 and 1992 the potency of the seized marijuana samples that the University of Mississippi analyzed averaged about three to three-and-half percent THC content, and that potency had been increasing thereafter, reaching about 7.3 or 7.4 percent in 2004.

Dr. ElSohly testified that the National Center cultivates marijuana by vegetative propagation, i.e., from cuttings, a technique that produces plants with the same genetic makeup as the mother plant. Dr. ElSohly also testified that the National Center has conducted research on indoor cultivation of marijuana, which enables the grower to control the environmental conditions in which the plants are grown, but that although the National Center could grow small amounts of marijuana indoors if the material it had in inventory did not meet the needs of a specific research project, it has not grown marijuana indoors for NIDA. Dr. ElSohly further testified that he had about 1,200 square feet available for indoor growing and that that space would permit him to grow tens of kilograms per year inside, as opposed to the hundreds of kilograms per year that he could grow outdoors on the National Center's twelve-acre plot.

Dr. ElSohly testified that the last time prior to the hearing that the National Center grew a marijuana crop at its outdoor facility was in 2001-2002, and that as of the date of the hearing he had enough marijuana in inventory, about a thousand kilograms, to cover what investigators needed.

The National Center's contract with NIDA specifies that the National Center's inventory of marijuana is to be maintained on a first-in, first-out system, i.e., that the oldest material is to be used first, unless the project officer at NIDA agrees to use newer material. Dr. ElSohly testified that the National Center keeps the marijuana it has cultivated in a secure vault in freezers to prevent the material from degrading over time.

Dr. ElSohly further testified that the National Center, as required by its contract with NIDA, conducts stability studies on the marijuana it cultivates to verify its potency after storage. Dr. ElSohly testified on cross-examination, however, that if he has two barrels of marijuana of the same composition, he will seek to use the newer material first, because "the fresher the material is, the better the material is."[41]

Dr. ElSohly testified that the National Center's marijuana crop is of various potencies, and that prior to the manufacturing process material of different potencies is mixed to achieve a batch of cigarettes of a consistent potency. According to Dr. ElSohly, the National Center has produced marijuana cigarettes with a potency of eight percent and bulk marijuana with a potency of thirteen or fourteen percent, and is capable of producing on a small scale (i.e., a few kilograms) marijuana with a potency of twenty percent or higher. Dr. ElSohly noted that the higher marijuana's potency, the more difficult it is to roll into cigarettes, but testified that he had been able to roll a batch of marijuana of six percent potency by machine and that the National Center had also made one batch of cigarettes with eight percent THC content when a researcher needed a higher-potency material that was too sticky to go through RTI's rolling machine.

Dr. ElSohly testified that the cannabichromene content of the marijuana available to researchers through NIDA is approximately .3 percent, and that the cannabidiol content ranges from about .1 percent to two percent.

3. About Research Triangle Institute

Kenneth Davis, Jr., Senior Program Director of RTI's Center for Chemistry Services, stated in a declaration that RTI is an independent non-profit organization formed in 1958 whose mission is scientific research and technology development to improve the human condition. RTI holds DEA registrations as a Schedule I through V manufacturer, including for bulk manufacture; as a Schedule I through V distributor; as a Schedule I through V importer, including in bulk; as a Schedule I through V exporter; as a Schedule I researcher; and as a Schedule II researcher. Mr. Davis oversees all of these registrations. Mr. Davis further stated that since 1968 RTI has produced and distributed marijuana cigarettes to researchers approved by the FDA, the DEA, and NIDA, and also has distributed marijuana cigarettes to patients in the experimental use program.

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[41] Transcript p. 1,573.

Mr. Davis further stated that RTI acquired the machine it uses to make marijuana cigarettes in 1976, that RTI gained technical expertise from North Carolina's tobacco industry, and that a dilemma the organization faced was how to produce cigarettes of varying potencies that are indistinguishable from each other. Mr. Davis stated that RTI receives barrels of manicured marijuana at about an 11.2 percent humidity level, processes the marijuana to reach a fifteen percent humidity level, and stores it in a cold room so it retains moisture. The marijuana is fed through a hopper into the rolling machine which, when it runs optimally, produces 800 to 1,000 cigarettes per minute.

Mr. Davis stated that RTI had produced thirty-two batches of machine-rolled cigarettes since the beginning of the NIDA marijuana project and that NIDA's needs and requests govern this production. Mr. Davis further stated that RTI had produced small batches consisting of 100 to 500 hand-rolled cigarettes, including a batch that was specified to be at eight percent potency, which is more challenging for mechanical rolling because material with a higher THC content is stickier. Mr. Davis stated that occasionally a researcher asks for bulk material, but that this is relatively rare.

Mr. Davis stated that RTI's goal is to develop and provide cigarettes that are consistent and standardized to meet the needs NIDA identifies, that RTI has received comments from NIDA about the quality of the cigarettes RTI produces, but that it had not received any comments since a few months before July 2002. Mr. Davis stated that RTI was able to respond to comments about the harshness of the marijuana it distributed by providing instructions on how to humidify it, that in 2001 the University of Mississippi added a machine that removed "the vast majority of seeds and stems"[42] from marijuana plant material, and that although initially RTI found this material too fine to go through its rolling machine, those problems were resolved and RTI has not received any recent complaints about seeds or stems in its finished products. Mr. Davis further stated that the ability to develop more potent material has been progressing, and that marijuana with eight percent THC content is available and marijuana with a content of ten percent THC could be accessible. Nonetheless, according to Mr. Davis, the project faced a challenge concerning the stability of higher-content THC material.

Finally, according to Mr. Davis, RTI had not, as of the date of his declaration

(January 6, 2006), received requests for marijuana products other than plant material, but had received inquiries about such products and would be willing and able to work on other delivery forms once it had "tool[ed] up."[43]

4. About the Multidisciplinary Association for Psychedelic Studies

The Multidisciplinary Association for Psychedelic Studies (MAPS) is a not-for-profit research and education organization that is tax-exempt pursuant to Section 501(c)(3) of the Internal Revenue Code. Its mission is to develop FDA-approved prescription drugs from Schedule I controlled substances and to educate the public about the risks and benefits of these substances. Richard Doblin, Ph.D., founded MAPS in 1986 and was its president as of the date of the hearing.

MAPS' 1,500 members include doctors, psychologists, and psychotherapists, as well as others who support scientific research into Schedule I drugs but would not necessarily use such research in their own professions. Dr. Doblin testified that psychedelic[44] drugs might have applications to treat conditions such as addiction (because such drugs may help addicts recognize their denial) or to enhance psychotherapy.

Dr. Doblin testified that most of the drugs that MAPS studies are not patent-protected, so pharmaceutical companies are not interested in funding research about them, and that these drugs are too controversial to attract government funding. Consequently, MAPS relies on private donors, including some foundations. Dr. Doblin further testified that ultimately, MAPS hopes to market the drugs it develops.

Dr. Doblin testified that MAPS' 2004 annual budget was about $800,000, and that there are about four full-time employees, plus researchers who are not employees but conduct studies pursuant to contracts with the organization. Dr. Doblin testified that probably at least one million of the roughly four million dollars that MAPS had spent in the four years prior to the hearing had been spent on research projects; that among other things, MAPS has sponsored studies of the use of ketamine (a Schedule III controlled

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[42] Declaration of Kenneth H. Davis, Jr., Jan. 6, 2006; Government exhibit 97, p. 3.
[43] Declaration of Kenneth H. Davis, Jr.; Government exhibit 97, p. 4.
[44] Dr. Doblin defined the word "psychedelic" as "mind-manifesting," i.e., revealing of the unconscious or subconscious, and testified that the term is not restricted to drugs, but also encompasses such things as dreams and meditation. Transcript p. 474.

substance) in treating alcoholics and heroin addicts and the use of methylenedioxymethamphetamine (MDMA) (a Schedule I controlled substance) for treatment of post-traumatic stress disorder; and that he was awaiting approval for a planned study of MDMA's potential use to treat anxiety in patients with terminal cancer. Dr. Doblin testified that MAPS also sponsored a study on using psilocybin (a Schedule I controlled substance) to treat obsessive-compulsive disorder, and that because neither NIDA nor the National Institutes of Mental Health was willing to sell psilocybin to use in the study, MAPS purchased it from a private producer at a cost of $12,250 for one gram.

Dr. Doblin testified to his personal belief "that marijuana should be a legal substance for both medical and non-medical purposes,"[45] that adults should be allowed to decide for themselves whether to use marijuana, and that prohibition on its use is counterproductive in reducing drug abuse. Dr. Doblin also acknowledged that as of the date of the hearing, he used marijuana recreationally approximately once per week, and that he started using marijuana in about 1971.[46] Dr. Doblin further testified that he considers smoked marijuana to be medicine, although he agreed that it has the potential for abuse. Dr. Doblin testified that although he thought that working through the FDA was the appropriate process in order to make marijuana into a medicine, the inability to obtain marijuana for research purposes has blocked that process.

5. About the Center for Medical Cannabis Research

Former California State Senator John Vasconcellos testified that after the voters of California adopted Proposition 215 in 1996,[47] he introduced legislation to establish the

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[45] Transcript p. 634.

[46] Respondent objected to this testimony at the hearing. I overruled the objection with the caveat that I might later decide that the testimony was irrelevant. Respondent renews the objection in his brief; I adhere to my ruling.

[47] Proposition 215 reads as follows:

> SEC. 1. Section 11362.5 is added to the California Health and Safety Code, to read:
> 11362.5. (a) This section shall be known and may be cited as the Compassionate Use Act of 1996.
> (b)(1) The people of the State of California hereby find and declare that the purposes of the Compassionate Use Act of 1996 are as follows:
> (A) To ensure that seriously ill Californians have the right to obtain and use marijuana for medical purposes where that medical use is deemed appropriate and has been recommended by a physician who has

University of California Center for Medical Cannabis Research (CMCR), hosted primarily at the University of California at San Diego and secondarily at the University of California at San Francisco. Mr. Vasconcellos testified that the establishing legislation required a scientific advisory committee to approve all proposals to conduct research funded by the CMCR, that all approved researchers were required to obtain appropriate federal licenses, and that research was ongoing as of the date of the hearing. Mr. Vasconcellos further testified that fifteen research projects had been selected and funded, but that as of the date of his testimony, there was no further state funding available. Mr. Vasconcellos testified that the purpose of the legislation was not to obtain FDA approval of marijuana as a drug, but "to demystify the roaring contentions of

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determined that the person's health would benefit from the use of marijuana in the treatment of cancer, anorexia, AIDS, chronic pain, spasticity, glaucoma, arthritis, migraine, or any other illness for which marijuana provides relief.

(B) To ensure that patients and their primary caregivers who obtain and use marijuana for medical purposes upon the recommendation of a physician are not subject to criminal prosecution or sanction.

(C) To encourage the federal and state governments to implement a plan to provide for the safe and affordable distribution of marijuana to all patients in medical need of marijuana.

(b)(2) Nothing in this section shall be construed to supersede legislation prohibiting persons from engaging in conduct that endangers others, nor to condone the diversion of marijuana for non-medical purposes.

(c) Notwithstanding any other provision of law, no physician in this state shall be punished, or denied any right or privilege, for having recommended marijuana to a patient for medical purposes.

(d) Section 11357, relating to the possession of marijuana, and Section 11358, relating to the cultivation of marijuana, shall not apply to a patient, or to a patient's primary caregiver, who possesses or cultivates marijuana for the personal medical purposes of the patient upon the written or oral recommendation or approval of a physician.

(e) For the purposes of this section, "primary caregiver" means the individual designated by the person exempted under this section who has consistently assumed responsibility for the housing, health, or safety of that person.

SEC. 2. If any provision of this measure or the application thereof to any person or circumstance is held invalid, that invalidity shall not affect other provisions or applications of the measure that can be given effect without the invalid provision or application, and to this end the provisions of this measure are severable.

contrary viewpoints and to find out by science carefully designed and commissioned and arbitrated by the protocols to find out whether, in fact, it's of any use."[48]

Mr. Vasconcellos opined that "people have a right to know more about what might help them in their suffering and pain or illness, whatever it might be and that the more research, the better, provided it's rigorous and according to protocol and objective and careful and approved by everybody who has to approve it."[49]

The enabling legislation for the CMCR, California Health and Safety Code § 11362.9, commissions the California Marijuana Research Program and directs it to "develop and conduct studies intended to ascertain the general medical safety and efficacy of marijuana and, if [marijuana is] found valuable, . . . develop medical guidelines for the appropriate administration and use of marijuana."[50] The statute further provides that:

> In order to ensure objectivity in evaluating proposals, the program shall use a peer review process that is modeled on the process used by the National Institutes of Health, and that guards against funding research that is biased in favor of or against particular outcomes. Peer reviewers shall be selected for their expertise in the scientific substance and methods of the proposed research, and their lack of bias or conflict of interest regarding the applicants or the topic of an approach taken in the proposed research. Peer reviewers shall judge research proposals on several criteria, foremost among which shall be both of the following:
> (1) The scientific merit of the research plan, including whether the research design and experimental procedures are potentially biased for or against a particular outcome.
> (2) Researchers' expertise in the scientific substance and methods of the proposed research, and their lack of bias or conflict of interest regarding the topic of, and the approach taken in, the proposed research.[51]

The legislation, among other things, establishes a Scientific Advisory Council and directs it to develop a scientific plan pursuant to which funds are to be allocated to various research studies and to review requests for funding;[52] specifies that the studies "include the greatest amount of new scientific research possible on the medical uses of,

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[48] Transcript p. 403.
[49] Transcript p. 406.
[50] CAL. HEALTH & SAFETY CODE § 11362.9(a)(2) (Deering 2005); Government exhibit 32.
[51] CAL. HEALTH & SAFETY CODE § 11362.9(c) (Deering 2005); Government exhibit 32.
[52] CAL. HEALTH & SAFETY CODE §§ 11362.9(e)(4), (p) (Deering 2005); Government exhibit 32.

and medical hazards associated with, marijuana;"[53] requires that the program "be limited to providing for objective scientific research to ascertain the efficacy and safety of marijuana as part of medical treatment, and should not be construed as encouraging or sanctioning the social or recreational use of marijuana";[54] and states that prior to approving any proposals, the program is to try to obtain research protocol guidelines from NIH and if NIH issues such guidelines, to comply with them.[55]

Dale Gieringer, Ph.D., is on the CMCR's National Advisory Council as a public interest member. He testified that the CMCR funds and coordinates studies on the medical use of marijuana, and that it is purely a research organization; it does not seek to develop drugs or bring them to market.

Dr. Doblin testified that he thought the CMCR had been able to obtain marijuana from NIDA for several studies because unlike MAPS, the CMCR was not trying to make marijuana into a prescription medicine. Dr. Doblin testified that as far as he knew, NIDA had supplied marijuana to all of the approximately fifteen projects that the CMCR had undertaken.

II. Work to Develop a Pharmaceutical Product from Marijuana

A. The Process of Developing a New Drug Product

Douglas Throckmorton, M.D., the Acting Deputy Director of FDA's Center for Drug Evaluation and Research (CDER), stated in an affidavit in evidence as a Government exhibit that the federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 321(g), defines "drug" in relevant part as:

> (A) articles recognized in the official United States Pharmacopoeia, official Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any articles specified in clause (A), or (B), or (C), ...[56]

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[53] CAL. HEALTH & SAFETY CODE § 11362.9(g) (Deering 2005); Government exhibit 32.
[54] CAL. HEALTH & SAFETY CODE § 11362.9(l)(3) (Deering 2005); Government exhibit 32.
[55] CAL. HEALTH & SAFETY CODE § 11362.9(m)(1) (Deering 2005); Government exhibit 32.
[56] Declaration of Douglas C. Throckmorton, M.D., August 17, 2005; Government exhibit 92, p. 1.

Dr. Throckmorton further stated that 21 U.S.C. § 321(p) of the Food, Drug, and Cosmetic Act, in relevant part, defines the term "new drug" as:

> (1) Any drug . . . the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof . . . or (2) Any drug . . . the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions.[57]

Dr. Throckmorton stated that in order for a drug to be generally recognized as safe and effective within the meaning of 21 U.S.C. § 321(p), a drug's "reputation must be based on adequate and well-controlled studies that establish that the drug is safe and effective";[58] the "studies must have been published in the scientific literature so that they are available to qualified experts";[59] and "qualified experts must generally recognize, based on those published studies, that the drug is safe and effective for its intended use."[60] Dr. Throckmorton further stated that even if an active ingredient in one drug product has been previously approved as safe and effective in another, the first drug product is considered a new drug if its particular formulation has not been previously approved or has not been found to be generally recognized as safe and effective. Dr. Throckmorton stated that any drug product derived from marijuana is a new drug within the meaning of 21 U.S.C. § 321(p) and that he was not aware of any evidence that any drug product derived from marijuana is exempt from the new drug requirements of the Food, Drug, and Cosmetic Act.

Dr. Throckmorton further stated that a new drug product may not be legally introduced into interstate commerce unless it has an approved new drug application (NDA), an approved abbreviated new drug application (ANDA), or a valid investigational new drug application (IND),[61] and that a new drug application is required

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[57] Declaration of Douglas C. Throckmorton, M.D.; Government exhibit 92, pp. 1-2.
[58] Declaration of Douglas C. Throckmorton, M.D.; Government exhibit 92, p. 2 (citing 21 C.F.R. § 314.126).
[59] Declaration of Douglas C. Throckmorton, M.D.; Government exhibit 92, p. 2.
[60] *Id.*
[61] *Id.* (citing 21 U.S.C. § 355).

to contain:

> (A) full reports of investigations which have been made to show whether or not such drug is safe for use and whether such drug is effective in use;
> (B) a full list of the articles used as components of such drug;
> (C) a full statement of the composition of such drug;
> (D) a full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of such drug;
> (E) such samples of such drug and of the articles used as components thereof as the Secretary may require; and
> (F) specimens of the labeling proposed to be used for such drug.[62]

Dr. Throckmorton stated that in order to develop the necessary reports showing that a particular drug product is safe and effective, the NDA sponsor must complete certain clinical investigations, i.e., experiments in which the drug is administered to, dispensed to, or used in one or more human subjects, and that clinical investigations of unapproved new drugs must be conducted under valid INDs.[63] The IND must include the name of the drug and all its active ingredients, its structural formula, the formulation of the dosage form, the route of administration, a summary of previous human experience with the drug, a description of the overall plan for investigating the drug product for the next year, and a protocol for the study. Dr. Throckmorton stated that INDs generally must:

> have a section describing the composition, manufacture, and control of the drug product. In each phase of the investigation sufficient information is required to be submitted to assure the proper identification, quality, purity, and strength of the investigational drug product. FDA recognizes that modifications to the method of preparation of a new drug substance and dosage form are likely as the investigation progresses. Final specifications for the drug substance and drug product are not expected until the end of the investigational process.[64]

Dr. Throckmorton described the three phases of the clinical investigation of a previously untested drug product as, in substance: Phase I, the initial introduction into humans, which is designed to determine the metabolic and pharmacologic actions of the drug in humans, the side effects associated with increasing doses, and if possible to obtain some evidence of effectiveness; Phase II, controlled clinical studies to explore the drug's effectiveness for a particular indication and determine its common short-term side

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[62] Declaration of Douglas C. Throckmorton, M.D.; Government exhibit 92, p. 3.
[63] *Id.* (citing 21 U.S.C. § 355(i) and 21 C.F.R. Part 312).
[64] Declaration of Douglas C. Throckmorton, M.D.; Government exhibit 92, pp. 3-4.

effects and risks; and Phase III, expanded controlled and uncontrolled clinical trials intended to obtain additional information about effectiveness and safety needed to evaluate the benefit-risk relationship and provide an adequate basis for labeling.

Irwin Martin, Ph.D., and David Auslander, Ph.D., testified on behalf of Respondent and the Government, respectively, as experts on new drug development. Dr. Auslander testified that at the end of Phase III of the investigation of a new drug, the sponsor submits the NDA to the FDA. Dr. Martin described the process of developing new drugs, starting with basic research: the discovery of a compound, an idea of how to use it, synthesis of the molecule, and testing in animals to show that it is pharmacologically active. Dr. Martin testified that once researchers conclude that the product is viable, a management team decides whether or not to test it in humans; if that decision is affirmative, the next step is assembly of a project team to work toward an IND, which is necessary in order to study the drug in humans.[65] Once the IND is in effect, according to Dr. Martin, the developers conduct Phase I studies in which the drug is tested in healthy volunteers to demonstrate its safety and its biopharmaceutical properties, i.e., how the body handles it. When the company concludes that it has sufficient data from these studies, it proceeds to Phase IIA, studies in which the drug is tried on a small group of patients who would be expected to benefit from it; in Phase IIB, the developers test the drug in larger groups of patients. Finally, in Phase III the drug is tested for safety in thousands of patients. [99] When the Phase III studies are complete the developers prepare and submit to the FDA an NDA summarizing the results of all of the studies.

Dr. Martin testified that the FDA takes up to ten months to review the NDA and approve the application or comment on it, and may seek additional information. Dr. Auslander added that after the sponsor of a drug development program provides the NDA, the FDA's Bureau of Compliance will conduct a pre-approval inspection to ensure that the facility designated in the NDA can produce the product as specified in the application. Dr. Martin further testified that often pharmaceutical companies conduct Phase IV studies, i.e., studies to gather additional information about a currently marketed

[65] Dr. Martin testified that an IND goes into effect in thirty days unless the FDA objects to it.

drug's safety and/or efficacy.

Dr. Martin testified that throughout the process of developing a drug, the developers maintain contact with the FDA, and that the entire process of drug development from identification of a likely compound to FDA approval averages about seven to eight years. Dr. Martin further testified that the ratio of INDs to approved NDAs is approximately ten to one, i.e., about ten percent of the drugs that undergo clinical testing are eventually marketed, but agreed with the comment in the Institute of Medicine's report that about one in five drugs that have been tested in humans obtains FDA approval for marketing. Dr. Martin further testified that a Tufts University research group estimated that it costs about $800 million (including opportunity costs) to successfully develop a new drug.[66]

Dr. Doblin testified that more than half of the $880 million estimate he provided of the cost of developing a new drug is opportunity cost, i.e., the cost of investing in research instead of something else, that this cost is calculated on assumptions that the rate of return on alternative investments would be twelve percent per year, compounded, and that it could take up to fifteen years to develop a drug. Dr. Doblin further testified that the calculation of opportunity costs also amortizes the costs of the projects that do not result in a marketable drug into the return of the projects that do.

Dr. Martin testified that in determining whether to develop a drug, pharmaceutical companies consider issues such as how many patients would have the condition or symptom that the drug would treat; how long such patients would use the drug; what competing products are already on the market; what research is being conducted by other companies on the same issue; and the patentability of the drug and/or its delivery system. Dr. Martin testified that assuring a reliable and consistent source of supply is critical to the development of a drug.

Dale Gieringer, Ph.D., is the California coordinator for the National Organization for the Reform of Marijuana Laws (NORML). Dr. Gieringer testified that the FDA requires anyone seeking approval of a drug to have a Drug Master File containing

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[66] Dr. Martin explained that this figure includes the research and development costs of those drugs that do not ever get to market, i.e., a company's total research and development costs divided by the number of NDAs approved in a year.

proprietary information such as the source of the drug under consideration, its production process, and evidence of its purity and quality.

Dr. Martin testified that scheduling of a drug as a controlled substance is a deterrent to its development because access to controlled substances is more restricted, physicians are disinclined to prescribe them, there may be a stigma associated with these drugs, the developer must incur additional expense for abuse liability studies, and the scheduling process at both the state and federal levels may result in expensive delays.

Dr. Martin testified that the FDA's criteria for approval of a drug are safety, efficacy (i.e., assurance that the drug does what it is supposed to do), and quality (the manufacturing controls that assure that the dosage form tested is the same as the one delivered to a patient).

B. Developing Botanical Products into Pharmaceuticals

Dr. Throckmorton defined botanical products as:

> finished, labeled products that contain vegetable matter as ingredients. Botanical products that meet the definition of a drug under 21 U.S.C. § 321(p) are subject to regulation as a drug. However, botanical drug products have certain unique characteristics that are taken into account in the application of FDA regulations. For instance, because of the complex nature of a typical botanical drug and the lack of knowledge of its active constituent(s), FDA may rely on a combination of tests and controls to ensure the identity, purity, quality, strength, potency, and consistency of botanical drugs.[67]

Dr. Martin noted that assuring quality is more complex for botanical products than for chemical ones, but that the FDA has issued a guidance document on how to submit an application for botanically derived material, thus indicating that the agency is willing to consider such applications.

The guidance document to which Dr. Martin referred is the Guidance for Industry, Botanical Drug Products (Botanical Drug Guidance), issued in June 2004 by the FDA's Center for Drug Evaluation and Research. The Botanical Drug Guidance explains when a botanical drug may be marketed as an over-the-counter product and when an NDA is required to market the drug. The Botanical Drug Guidance also contains nonbinding recommendations to sponsors on submitting INDs for botanical drug products. The Botanical Drug Guidance includes among the information that should be provided for

[67] Declaration of Douglas C. Throckmorton, M.D.; Government exhibit 92, p. 5.

botanical drug substances qualitative and quantitative descriptions of the substance, including the quantities of the active constituents, and the physical and chemical properties, biological activity, and clinical indications of the botanical raw material. The Botanical Drug Guidance also specifies that both a biological activity and chemical assay should be performed if the botanical drug substance is potent, toxic, addictive, or has abuse potential, and specifically lists marijuana as having abuse potential.

Dr. Auslander testified that there is a difference between synthetic material of established purity and defined attributes, and botanicals, which are much more complex. Dr. Auslander further testified that the FDA recognizes the difficulties of going through its approval processes for botanical materials by permitting different approaches, such as fingerprinting and markers, than are used in synthetic products. Dr. Auslander testified that a marker is a response to chromatography that does not match the response of the source, i.e., a surrogate for some material believed to be active; that the FDA expects this material to be consistently present in the botanical product being studied; that the markers are quite important; and that at the advanced clinical stage, Phase III, the FDA would want them to be characterized and quantified.

Dr. Auslander testified that the "fingerprints" of a material are determined by spectroscopic and chromatographic procedures and provide a better understanding of what the material looks like and how it should behave. Dr. Auslander testified that chemical assay is a quantitative as opposed to qualitative analysis: "Qualitative just says this material exists. A chemical assay or quantitative assay will give you the evidence this material exists to what extent, how much of it exists."[68] Dr. Auslander noted that the FDA accepts the proposition that the chemical assay of a botanical material may not be feasible at the early stage and that it is sufficient to say that specific materials exist in the product without determining the extent to which they are present. Dr. Auslander testified that a biological assay is an alternative approach to analyzing botanical products and consists of administering the material to an animal and assessing the results.

Dr. Auslander testified that the Botanical Drug Guidance calls for an IND for a botanical to include a qualitative description, i.e., a description of what the material is and what it purports to be, of the drug substance that is the subject of the clinical program, as

opposed to a quantitative description, and would also include its biological activity and clinical indications, if known.

Dr. Auslander testified that potency relates to chemistry and manufacture control, and is in a sense a measure of the purity of the substance; efficacy pertains to whether the drug has the desired effects; and safety is the consideration of avoiding undesirable effects. Dr. Auslander testified that because botanical products are more complex than synthetic ones, it is more complicated to achieve the consistent quality necessary for efficacy and safety, and that the more active constituents a botanical product has, the more complicated it is. Dr. Auslander testified that some of the complications arising from using botanicals can be alleviated by extracting from them the active ingredient needed for development of a pharmaceutical product. However, Dr. Auslander noted that although extraction is always theoretically feasible, it may require a tremendous effort.

Dr. Auslander testified that his understanding of the Botanical Drug Guidance is that if the product is potent, highly active, toxic, addictive, or has abuse potential, the FDA "really wants"[69] either a biological or chemical assay. Dr. Auslander further testified that if the sponsor of a proposed new botanical product switched to a different source during the IND process, the sponsor would need to update the IND and submit the update to the FDA. Dr. Auslander testified that Phase I and II clinical studies would not necessarily have to be repeated if the sponsor switched sources, but the sponsor would have to show that the material from the two sources was equivalent. Dr. Auslander testified that it "would be a major exercise to go from source A to B during the advanced clinical trials, in particular where efficacy and safety profiles are being established. It would not be a trivial experience. It would be a major undertaking."[70]

Dr. Doblin testified that cloning enables reproduction of a plant's chemical composition, and that the FDA has held that it is acceptable to assess a plant's safety and efficacy by testing the plant as a whole, not each of its constituent compounds. Dr. Doblin noted that although there are probably more than 400 chemical compounds in marijuana, the FDA has developed guidelines for developing other botanical products

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[68] Transcript p. 2,012.
[69] Transcript p. 2,016.
[70] Transcript p. 2,029.

with similar numbers of compounds in them. Dr. Voth testified that marijuana's chemistry is known, and that although he did not think it was impossible to reproduce marijuana's chemistry, it would be difficult.

C. Evidence About Developing Pharmaceutical Products from Marijuana and/or Its Components

1. Background

In testimony before the Subcommittee on Criminal Justice, Drug Policy, and Human Resources, Committee on Government Reform, of the House of Representatives on April 1, 2004, Robert J. Meyer, M.D., Director of the Office of Drug Evaluation II of FDA's Center for Drug Evaluation and Research, described the FDA's process for demonstrating the safety and efficacy of new drugs and also discussed research with marijuana. Dr. Meyer stated that the Department of Health and Human Services and FDA:

> support the medical research community who intend to study marijuana in scientifically valid investigations and well-controlled clinical trials, in-line [sic] with the FDA's drug approval process. HHS and FDA recognize the need for objective evaluations of the potential merits of cannabinoids for medical uses. If the scientific community discovers a positive benefit, HHS also recognizes the need to stimulate development of alternative, safer dosage forms. In February 1997, an NIH-sponsored workshop analyzed available scientific information and concluded that "in order to evaluate various hypotheses concerning the potential utility of marijuana in various therapeutic areas, more and better studies would be needed."[71]

Dr. Meyer further stated that "FDA will continue to be receptive to sound, scientifically-based research into the medicinal uses of botanical marijuana and other cannabinoids. FDA will continue to facilitate the work of manufacturers interested in bringing to the market safe and effective products."[72]

In her April 1, 2004 testimony before the House subcommittee, Dr. Volkow noted the 1999 Institute of Medicine report discussed above, as well as the results of a two-day meeting convened by NIH in February 1997 that examined the research on the medical

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[71] Testimony by Robert J. Meyer, M.D., Director, Office of Drug Evaluation II, Center for Drug Evaluation and Research, FDA, before the Subcommittee on Criminal Justice, Drug Policy, and Human Resources of the House Committee on Government Reform (April 1, 2004); Respondent exhibit 54, p. 4.

[72] *Id.*; Respondent exhibit 54, p. 5.

uses of marijuana and its constituents, and stated that:

> Both reports found that there are too few scientific studies to determine marijuana's therapeutic utility, but that research is justified into marijuana's use for certain conditions or diseases including pain, neurological and movement disorders, nausea in patients who are undergoing chemotherapy for cancer, and loss of appetite and weight (cachexia) related to AIDS.[73]

Dr. Volkow further stated that subsequent to these reports, NIH had supported two studies on marijuana for medical use, one on the effects of smoked marijuana on HIV levels, appetite, and weight loss associated with HIV-related wasting syndrome; and the other on the effects of smoked and oral THC on HIV-infected individuals with unintended weight loss. Dr. Volkow noted that as of the date of her statement, the Department of Health and Human Services had approved seventeen clinical or preclinical studies undertaken by CMCR.

Dr. Volkow also stated that recent research had discovered a major class of cannabinoid receptors in the brain and another class found mostly on immune system cells, and that the brain receptor system was yielding insights into how marijuana disrupts memory traces. She added that recent research showed connections between the cannabinoid system and neuronal processes connected to relapse into cocaine abuse.

As noted above, the Institute of Medicine report on medicinal use of marijuana stated that purified cannabinoid compounds would be preferable as medicine to marijuana. Dr. Doblin testified that he disagreed with this statement because the botanical product may have ingredients with synergistic effects or ingredients that moderate the toxicity of other ingredients, but pharmaceutical companies may prefer to market only the isolated ingredients, which they can patent.

As also noted above, the Institute of Medicine report concluded that in most cases there are more effective medications than cannabinoids. Dr. Doblin testified, however, that marijuana seems to have a substantial effect in controlling nausea for some cancer chemotherapy patients when other medications do not work, and marijuana substantially stimulates appetite for some patients with AIDS wasting syndrome, and sometimes

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[73] Statement of Nora D. Volkow, M.D., Director, National Institute on Drug Abuse, National Institutes of Health, U.S. Department of Health and Human Services, before the Subcommittee on Criminal Justice, Drug Policy, and Human Resources of the House Committee on Government Reform (April 1, 2004); Government exhibit 31, p. 3.

controls pain that other medications do not.

2. NIDA, MAPS, and Developing a Pharmaceutical Product from Marijuana

NIDA holds and submits to the FDA the Drug Master File for the marijuana grown by the National Center. Dr. Gieringer testified that marijuana from the NIDA supply could not be used for an NDA because the developer would not have control over the drug – NIDA would, and thus NIDA or the contractor who grows marijuana for NIDA, rather than the developer, would have the Drug Master File for it. Dr. Gieringer acknowledged that NIDA could decide to develop a drug from the marijuana grown under contract with it, but testified that it would not make sense for a commercial company to rely on a supply of marijuana from NIDA because the company could not control the supply. Dr. Gieringer also emphasized that NIDA has stated that its mission does not include studying the medical uses of marijuana or advocating for support of research on such uses.

Dr. Doblin testified that MAPS was not doing any marijuana research because of the inability to obtain the drug, but that he thought that if MAPS had its own supply, it could raise the five to ten million dollars that it would cost to make marijuana into medicine, noting that more than fifteen million dollars had been spent on medical marijuana initiatives in various states. Dr. Doblin testified that he did not think that any for-profit pharmaceutical companies were working on making marijuana into medicine because it would be difficult to patent and because of the political obstacles to that effort.

Dr. Doblin testified that safety studies of potential new drugs analyze safety in thousands of patients, but that various governments have already assessed the risks of marijuana and these assessments are available in the scientific literature, so that the safety of marijuana could be tested on a much smaller group of 500 to 600 patients. In addition, Dr. Doblin testified, because MAPS is a non-profit organization, it has lower overhead and receives donated labor, and researchers work for non-profit organizations for less than they would charge for-profit pharmaceutical companies.

With respect to the factors to consider in determining whether marijuana has an accepted medical use, Dr. Doblin testified that he thought: (1) marijuana has a known and reproducible chemistry, as indicated by the FDA's acceptance of NIDA's Drug Master File; (2) there have not been adequate safety studies for the FDA to make marijuana into

medicine; (3) there have not been adequate efficacy studies; (4) there are qualified experts who have accepted marijuana as a medicine; and (5) there is substantial and widely available scientific evidence.

Dr. Doblin testified that the process for rescheduling a Schedule I drug requires adequate and well-controlled studies of both its safety and efficacy and then convincing the FDA that "you've demonstrated a balance of safety and efficacy that suggests that [the drug at issue] should be approved."[74] Dr. Doblin further testified that once the FDA has approved a Schedule I drug as a prescription medicine, it is up to the DEA to determine in which schedule the drug belongs.

D. Dr. ElSohly's Work with Marijuana Other Than for NIDA

Dronabinol is a synthetic form of THC and is a Schedule III controlled substance; Marinol is the brand name for a drug made from dronabinol and is used to enhance appetite and treat nausea.[75] Dr. ElSohly testified that there is currently one manufacturer of synthetic THC and that this company has an exclusive license with the manufacturer of Marinol and cannot produce the synthetic product for anyone else. Dr. ElSohly further testified that it would be very difficult for someone else to develop a new process to make synthetic THC and establish the facility to manufacture it, and that, consequently, a good alternative is to extract and purify THC from plant material.

The National Center also grows marijuana to prepare extracts that Tyco Healthcare, a division of Mallinckrodt, uses to develop pharmaceutical products. This marijuana is grown on the same plot on which the marijuana for NIDA is grown and could have a THC content as high as twenty-three percent.

In October 1999 the DEA and the National Center entered into a Memorandum of Agreement that permitted the National Center to develop THC in a pharmaceutically acceptable dosage form suppository and to provide a crude THC extract for further purification by a DEA-registered manufacturer. The memorandum noted, among other things, that the Single Convention prohibits private trade in marijuana, but that it does not prohibit private trade in "cannabis preparations," which would include the extract that the

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[74] Transcript p. 627.

[75] Dr. Voth testified that marijuana is most often abused in its plant form, and that he had not determined any significant abuse of dronabinol or Marinol in the United States.

National Center was developing. Consequently, the memorandum permitted the National Center to distribute THC extract to private entities as long as it complied with the Controlled Substances Act and DEA regulations.

By letter dated June 15, 2005, the DEA granted the National Center a manufacturing quota for 2005 of 4,500 kilograms for Mallinckrodt to use to produce a generic THC product. As of the date of the hearing, according to Dr. ElSohly, the National Center had about one thousand kilograms of bulk plant material in inventory for extract production, which he hoped would be used in suppositories that were in Phase I clinical trials.

Dr. ElSohly has patented processes to isolate THC from marijuana plant material, to convert THC to various ester analogs, to formulate suppositories containing readily available THC, to identify the country of origin of marijuana, and to prepare cannabichromene.

Dr. ElSohly is also the president and laboratory director of ElSohly Labs, Incorporated (ElSohly Labs), an analytic forensic laboratory in Oxford, Mississippi.

III. The Events Leading Up to Respondent's Application

A. About Research Utilizing Marijuana

The parties stipulated that "research continues about how cannabis may be of therapeutic benefit to patients."[76]

Dr. ElSohly testified that preclinical research encompasses the work performed before a drug is introduced into humans, e.g., chemical analysis, study of animal toxicology, or study of animal pharmacology; and that clinical research refers to studies of the drug in humans. Most of the research discussed in this proceeding was clinical research in humans and was undertaken using marijuana supplied by the National Center as authorized by NIDA.

As discussed above, the National Center cultivates marijuana pursuant to a contract with NIDA and supplies it to RTI, which rolls the marijuana into cigarettes and ships them to researchers as directed by NIDA. If research utilizing marijuana is funded by NIDA, the marijuana is provided free of charge; researchers who have approval to use

[76] Prehearing Ruling issued May 23, 2005; ALJ exhibit 5, p. 1.

marijuana but who are not federally funded are required to pay for the marijuana at a price set by NIDA.

The National Center produces marijuana with various contents of THC, including placebo material.[77] Dr. ElSohly testified that this material is prepared by extracting all the THC and other cannabinoids from active marijuana, but that the resulting material is rather dry and does not smell or taste like cannabis, and so experienced marijuana smokers can infer that they are getting placebo. Consequently, Dr. ElSohly was asked to develop a variety of the marijuana plant that would have almost no cannabinol, but would have the other components so that it would smell and appear more like active marijuana.

B. MAPS' Research Efforts

1. MAPS' Work with Donald Abrams, M.D.

Dr. Doblin testified that for his master's thesis he surveyed oncologists about the differences between Marinol and smoked marijuana, and that his study showed that some oncologists found smoked marijuana was more effective than Marinol in controlling nausea resulting from chemotherapy. Dr. Doblin further testified that after the FDA approved Marinol as a prescription medicine, research into smoked marijuana came to a halt, but he eventually contacted Donald Abrams, M.D., a leading researcher on acquired immune deficiency syndrome (AIDS), and worked with him to develop a protocol that eventually received the requisite authorizations to study marijuana's potential benefits for AIDS patients. Dr. Doblin testified that when Dr. Abrams applied to NIDA to purchase marijuana, NIDA did not act on his application for nine months and then declined to provide the marijuana.

By letter dated April 28, 1995, Dr. Abrams wrote to the then-Director of NIDA, responding to various concerns apparently raised by NIDA and expressing disappointment at NIDA's denial of his application. The letter stated, in part:

> As an AIDS investigator who has worked closely with [the] National Institutes of Health and the U.S. Food and Drug Administration for the past 14 years of this

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[77] Dr. ElSohly testified that the placebo effect occurs when a subject thinks he is feeling the effects of a drug although he is not taking that drug but, rather, a product that does not contain the drug's active ingredient. Dr. ElSohly testified that in studies using marijuana placebo, the subjects rotate among using low-THC, high-THC, and placebo cigarettes, reporting on the effects of each use but not knowing which product they are using.

> epidemic, I must tell you that dealing with your Institute has been the worst experience of my career! The lack of any official communication for nine months is unheard of, even in the most cumbersome of government bureaucracies.[78]

Dr. Doblin testified that MAPS and Dr. Abrams attempted to obtain marijuana from a licensed company in the Netherlands, but that although the DEA said that an export permit from the Dutch government was a prerequisite to DEA approval, the Dutch government said it wanted the DEA to issue the import permit first, and in the end the marijuana was not imported. By letter dated May 10, 1995, Dr. Doblin asked Dr. ElSohly to supply marijuana for Dr. Abrams' study. By memorandum dated May 12, 1995, Dr. Doblin advised that he thought Dr. Abrams would also be willing to test a marijuana suppository on which Dr. ElSohly held a patent[79] if Dr. ElSohly could arrange for funding for the extra costs.

By memorandum dated May 24, 1995, Dr. Doblin advised Dr. Abrams that the Public Citizen Litigation Group had offered to help him challenge NIDA's decision not to provide marijuana for the proposed study and had suggested that Dr. Abrams file a Freedom of Information Act request pertaining to that decision. On May 25, 1995, Dr. Doblin sent a fax to Dr. ElSohly advising him that Dr. Abrams had agreed to expand the proposed study to include a group of patients who would receive a suppository, if Dr. ElSohly could fund that portion of the study and make appropriate marijuana available, and if Dr. Abrams could secure approval for that portion of the study from the various authorities who had already approved the initial proposal. Dr. ElSohly testified that he received the May 10, May 12, and May 25, 1995 letters but that he could not find any record of his responses, and that he was not sure whether he responded or not. Dr. ElSohly further testified that he did not feel that he could provide material for studies outside of his contract with NIDA because NIDA owned the marijuana he cultivated and because the contract required him to provide marijuana only to NIDA-approved researchers.

On June 1, 1995, Dr. Doblin wrote to Lester Grinspoon, M.D., advising him about

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[78] Letter from Donald I. Abrams, M.D., to Alan I. Leshner, Ph.D. (April 28, 1995); Respondent exhibit 15.

[79] Dr. Doblin testified that he did not think that at this point Dr. ElSohly had conducted any study of this suppository on humans and that the effort to develop the suppository was separate from Dr. ElSohly's contract with NIDA.

Dr. Doblin's efforts to obtain marijuana from a Swiss producer and about a representative of that producer's comments that he did not think the Swiss Minister of Health would "stand up to the DEA and authorize the export of marijuana"[80] to the United States. In that same memorandum, Dr. Doblin advised that he had not heard from Dr. ElSohly about obtaining marijuana from the National Center.

Eventually, Dr. ElSohly declined to provide marijuana for the study and Dr. Abrams did not undertake it. However, according to Dr. Doblin, following passage of California's Proposition 215 in 1996, NIDA contacted Dr. Abrams and said it would be interested in a study of the risks of marijuana use by HIV-positive patients. Dr. Abrams accepted this offer and NIDA provided the marijuana and one million dollars in funding. Dr. Doblin testified that the study showed that marijuana use did not hurt the immune system, increase viral load (the amount of virus in the blood), or negatively interact with the protease inhibitors[81] that the study subjects were taking, and that the subjects increased their caloric intake and gained weight.

Dr. Doblin also noted that the use of protease inhibitors had reduced the incidence of AIDS wasting in the United States, and that Dr. Abrams had concluded that rather than revisiting the rejection of his protocol on that subject, he would more effectively spend his research efforts on other clinical issues.

2. MAPS' Work with Ethan Russo, M.D.

Dr. Doblin testified that after NIDA refused to supply marijuana to Dr. Abrams, Dr. Doblin began working with Ethan Russo, M.D., a neurologist seeking funding from NIDA for a study on treating migraines with marijuana. Dr. Doblin testified that over about a four-year period, from roughly 1996 to 1999, NIDA rejected Dr. Russo's protocol several times and eventually Dr. Russo submitted his protocol to the FDA and to his own institutional review board, both of which approved it, but NIDA refused to supply marijuana. Dr. Doblin testified that as of the date of the hearing, Dr. Russo had been hired by a pharmaceutical company as a scientific advisor, and therefore could not do any further work on marijuana independently of that company.

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[80] Memorandum from Richard Doblin, Ph.D., to Lester Grinspoon, M.D. (June 1, 1995); Respondent exhibit 33.

[81] Protease inhibitors apparently inhibit replication of the virus.

3. The Orphan Drug Designation

By letter dated May 25, 1999, FDA's Office of Orphan Products Development notified Dr. Doblin that it had approved MAPS' application for designation of marijuana as an orphan drug[82] for the treatment of HIV-associated wasting syndrome. Dr. Doblin testified that MAPS has not been able to use this orphan drug designation because it has not been able to obtain marijuana from NIDA. According to Dr. Doblin, developing marijuana into a prescription medicine "is MAPS' explicit goal, so therefore, I think that sends up red flags, and anything that we do gets shut down."[83]

4. MAPS' Work with Chemic

Dr. Doblin testified that burning marijuana, as occurs when it is smoked, releases products that may be harmful, and that it seemed clear that developing a way to vaporize marijuana would be a step toward making the end product less irritating to the lungs. Consequently, according to Dr. Doblin, he felt it necessary to try to develop a vaporizing device that would deliver marijuana without combustion, and he and Dr. Gieringer initially looked at water pipes, using marijuana supplied by NIDA. Dr. Doblin testified that this study showed that water pipes filtered out cannabinoids as well as particulate matter, and that the various ingredients were in similar proportions in the water pipe smoke to what they were in the traditionally produced smoke.

Consequently, Dr. Doblin started working with Chemic Labs (Chemic), a DEA-registered laboratory that performs research under contract to pharmaceutical companies, so that Chemic could conduct research on using a vaporizer as a delivery device for marijuana. Chemic applied to NIDA for ten grams of marijuana and also applied to import ten grams from the Netherlands to use in studies to determine the consequences of

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[82] Dr. Doblin testified that an orphan drug designation carries tax incentives that do not apply to a non-profit organization like MAPS, but that it also sometimes causes the FDA to accept data from smaller groups of patients than it would require for other drugs. Dr. Throckmorton stated that dronabinol was given orphan drug designation for the stimulation of appetite and the prevention of weight loss in AIDS patients in 1991, but that this designation has no bearing on whether any other drug containing any component of marijuana will receive orphan drug designation in the future. Dr. Throckmorton also noted that determination of orphan drug status is made as of the time the request is made, and that a condition that meets the criteria of a rare disease at one point in time may not continue to meet those criteria in the future.

[83] Transcript pp. 689-690.

using the vaporizing device; according to Dr. Doblin, the NIDA marijuana had almost no cannabidiol but the Dutch marijuana did. Dr. Doblin testified that the purpose of this study was solely to test the device; no human use of marijuana was involved.

On May 19, 2004, Dr. Doblin wrote to Dr. Volkow, the Director of NIDA, protesting its failure to act on Chemic's application to purchase the ten grams of marijuana. According to Dr. Doblin's letter, Chemic Labs had filed its application on June 24, 2003, and applied to the DEA for an import permit for the Dutch marijuana on the same date. By letter dated June 9, 2004, Dr. Volkow responded to Dr. Doblin, advising that:

> As you know, NIDA is just one of the participants on the HHS review panel and continues, on behalf of the U.S. Government, to provide supplies of well-characterized cannabis for both NIH and non-NIH-funded research. The latter is conducted according to the procedures established in 1999 by HHS for obtaining access to marijuana for research purposes. It is not NIDA's role to set policy in this area or to contribute to the DEA licensing procedures. Moreover, it is also not NIDA's mission to study the medicinal uses of marijuana or to advocate for the establishment of facilities to support this research. Therefore, I am sorry but I do not believe that we can be of help to you in resolving these concerns.[84]

Shortly before the hearing in the instant case, NIDA rejected Chemic's application. In a letter to Chemic dated July 27, 2005, Joel Egertson, apparently Assistant Secretary for Health, Office of Public Health and Science of the Department of Health and Human Services, advised Chemic's president that the Department of Health and Human Services' program for providing marijuana for research focused on clinically meaningful research, and that a committee of scientists from the Public Health Service had concluded that the proposed project would not add significantly to the scientific knowledge base, that the rationale for each aim of the proposal was not clearly defined in the proffered protocol, and that the significance of the study with respect to furthering the field of knowledge and the study's clinical potential were not presented. Consequently, the committee recommended that NIDA not provide marijuana for the study.

Chemic responded by letter dated September 9, 2005, emphasizing, among other things, that the study it proposed to undertake was not a clinical investigation, and that it wished to evaluate differing vaporization efficiencies of cannabidiol and cannabinol.

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[84] Letter from Nora D. Volkow, M.D., to Richard Doblin, Ph.D. (June 9, 2004); Respondent exhibit 13.

Dr. Doblin testified that Chemic did not intend to redesign its protocol, but would challenge NIDA's conclusion that it was not scientifically meritorious. Dr. Doblin further testified that Chemic had applied for DEA registration to import marijuana and as a researcher and that the study was intended both to compare the Dutch marijuana to that produced for NIDA and to evaluate the vaporizer in terms of the consistency of its performance. Dr. Doblin testified that because this study would not involve testing on humans, no FDA approval is required, but that MAPS needed Public Health Service and NIDA approval to obtain the marijuana.

5. Dr. Doblin's Obtaining of Marijuana via the Drug Detection Laboratory

Dr. Doblin testified that the Drug Detection Laboratory in Sacramento, California, has permission from the DEA to accept samples of drugs from anonymous senders, and that he arranged for the Drug Detection Laboratory to send some marijuana to Chemic for the vaporizer studies described above. Dr. Doblin testified that he thought that the Drug Detection Laboratory was authorized to send marijuana to Chemic.

Dr. Doblin testified that he had "multiple relationships"[85] with the Drug Detection Laboratory and that, among other projects, he had made it publicly known that he would like some marijuana that patients in the compassionate use program had received from NIDA to be sent to the Drug Detection Laboratory so that its potency could be compared with that of marijuana from marijuana buyers' clubs. An unidentified compassionate use patient sent marijuana to the Drug Detection Laboratory, which analyzed it and then sent it, at Dr. Doblin's behest, to Chemic. Dr. Doblin testified that Jeff Zender, the head of the Drug Detection Laboratory, told him that representatives of the DEA talked to him about this incident; according to Dr. Doblin, "I didn't get the impression that it was necessarily forbidden, but I certainly got the impression that what we want to do was to go directly to NIDA, that that would be a preferable approach. And that's what we've done."[86]

C. About Current Arrangements to Supply Marijuana for Research

Dr. ElSohly testified that researchers wanting to utilize marijuana in their studies must seek it from NIDA, and that if NIDA approves the request, it directs Dr. ElSohly either to ship bulk material from his facility or to direct RTI to ship marijuana cigarettes.

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[85] Transcript p. 670.

Dr. Gust, the Special Assistant to NIDA's Director, testified that there are suppliers in addition to NIDA for some Schedule I controlled substances, but that for many of these substances NIDA is the sole supplier. Dr. Gust testified that he did not know whether there was any requirement that NIDA be the sole source for any Schedule I substances other than marijuana.

Dr. Gust testified that when a request for any controlled substance that NIDA provides for research is sent to the Drug Supply Program, there are three steps that must be completed: 1) the research proposal must undergo a peer review for scientific merit; 2) the researcher must obtain a DEA registration; and 3) the researcher must file an IND with the FDA. Upon completion of these requirements, the researcher submits a DEA order form to NIDA to obtain the marijuana.

According to an NIH Guidance released May 21, 1999, and still in effect as of the date of the hearing, NIDA evaluates non-NIH-funded studies as to scientific quality, the quality of the organization's peer-review process, and the objectives of the proposed research. The introduction to the NIH Guidance advises:

> The intent of this document is to provide guidance to the biomedical research community who intend to study marijuana in scientifically valid investigations and well-controlled clinical trials on the procedures of the Department of Health and Human Services (HHS) for providing research-grade marijuana to sponsors.[87]

Specifically, the NIH Guidance lists as factors it will consider in determining whether to provide marijuana:

> The extent to which the protocol incorporates the elements of good clinical and laboratory research; the extent to which the protocol describes an adequate and well-controlled clinical study to evaluate the safety and effectiveness of marijuana and its constituent cannabinoids in the treatment of a serious or life-threatening condition; the extent to which the protocol describes an adequate and well-controlled clinical study to evaluate the safety and effectiveness of marijuana and its constituent cannabinoids for a use in which there are no alternative therapies; the extent to which the protocol describes a biopharmaceutical study designed to support the development of a dosage form alternative to smoking; [and] the extent to which the protocol describes high-quality research designed to address basic, unanswered scientific questions about the effects of marijuana and its constituent

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[86] Transcript p. 677.

[87] National Institutes of Health, Announcement of the Department of Health and Human Services' Guidance on Procedures for the Provision of Marijuana for Medical Research (May 21, 1999); Government exhibit 24, p. 1.

cannabinoids or about the safety or toxicity of smoked marijuana.[88]

The NIH Guidance also specifies that the goal of the program "must be to determine whether cannabinoid components of marijuana administered through an alternative delivery system can meet the standards enumerated under the federal Food, Drug, and Cosmetic Act for commercial marketing of a medical product . . . ."[89] Dr. Gust testified that the Public Health Service review process would thus favor research on the derivatives of the marijuana plant and non-smoked delivery systems, but he also testified that research with the plant material and smoked marijuana is a necessary first step prior to research purifying marijuana's components and developing alternative delivery systems.

The NIH Guidance also states, quoting the Institute of Medicine report referenced above, that "'the purpose of clinical trials of smoked marijuana would not be to develop marijuana as a licensed drug, but such trials could be a first step towards the development of rapid-onset, non-smoked cannabinoid delivery systems.'"[90] Dr. Gust testified that he could not say that research seeking to develop marijuana as a licensed drug would be inconsistent with that goal, because that issue would be a question for the FDA rather than for NIDA, and he observed that the sentence quoted was from the Institute of Medicine, not the Public Health Service. Dr. Gust also testified, however, that "there is a strong endorsement of this concept within NIH and HHS that ultimately there's going to be pharmaceuticals developed based on the components of marijuana, that there will be purified pharmaceuticals. They won't be in a smoked product, and they'll probably develop to be administered through alternative delivery devices."[91]

The NIH Guidance further states:

> The focus of HHS's program is the support of quality research for the development of clinically meaningful data. HHS intends to make available a sufficient amount of research-grade marijuana to support those studies that are the most likely to yield usable, essential data. However, it should be noted that NIDA's supply of marijuana is subject to a number of constraints associated with the cultivation of a research-grade crop and that the supply at times may be

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[88] *Id.*; Government exhibit 24, pp. 2-3.
[89] *Id.*; Government exhibit 24, p. 2.
[90] *Id.*
[91] Transcript p. 1,706.

variable.[92]

The NIH Guidance interprets Articles 23 and 28 of the Single Convention as providing "that if a country allows cultivation of the cannabis plant for research purposes, the country must establish a national agency to control the cultivation and distribution of the crop."[93] The Guidance goes on to note, "Currently, the National Institute on Drug Abuse (NIDA), a component of the National Institutes of Health (NIH), oversees the cultivation of research-grade marijuana on behalf of the United States Government."[94]

Dr. Gust testified that the NIH Guidance applies to applications to do research on medical uses of marijuana in human patients, and thus does not apply to basic research, some animal research, or research in healthy human volunteers. Dr. Gust further testified that NIDA does not have expertise in reviewing applications involving the use of controlled substances for treatment of disease, because such studies do not fall within NIDA's mission, so the Department of Health and Human Services moved the review of such applications to the Public Health Service. Dr. Gust acknowledged that Public Health Service review is required only for research proposals seeking to utilize marijuana, and not for other Schedule I drugs made available through NIDA's Drug Supply Program or for controlled substances not provided by the federal government. Dr. Gust testified that the members of the Public Health Service Review Committee are from the Public Health Service's component agencies, and are drawn primarily from FDA, NIH, and SAMHSA.[95]

Dr. Gust testified that a researcher seeking NIH funding for research with marijuana undergoes an NIH peer review process as part of the application for funding; a privately-funded researcher seeking to obtain marijuana for non-medical research undergoes an ad hoc review conducted by NIDA; and a researcher seeking marijuana for medical research undergoes the Public Health Service peer review. A researcher who does not request controlled substances from NIDA does not undergo any review from

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[92] National Institutes of Health, Announcement of the Department of Health and Human Services Guidance on Procedures for the Provision of Marijuana for Medical Research (May 21, 1999); Government exhibit 24, p. 2.
[93] *Id.*; Government exhibit 24, p. 1.
[94] *Id.*
[95] Dr. Gust testified that the committee, and not NIDA's director or deputy director, makes the final decision as to scientific merit.

that agency, but does undergo an FDA review. Dr Gust testified that the FDA process focuses primarily on safety rather than scientific merit, although he acknowledged that the NIH Guidance states that:

> FDA's primary objectives in reviewing an IND are, in all phases of the investigation, to assure the safety and rights of subjects, and, in Phase 2 and 3, to help assure that the quality of the scientific evaluation of drugs is adequate to permit an evaluation of the drug's effectiveness and safety. Therefore, although FDA's review of Phase 1 submissions will focus on assessing the safety of Phase 1 investigations, FDA's review of Phases 2 and 3 submissions will also include an assessment of the scientific quality of the clinical investigations and the likelihood that the investigations will yield data capable of meeting statutory standards for marketing approval.[96]

Dr. Gust testified that the Public Health Service review process generally takes three to six months.

Dr. Gust testified that in determining whether to provide marijuana for a study, the Public Health Service committee follows a similar procedure to that NIH uses in assessing the scientific merit of a proposal submitted to it for funding: NIH's peer review committees first determine which proposed projects they will not further consider and then review all the other proposals and assign them a grade from one to five, with one being the highest score. The projects are then considered for funding by the NIH institute to which they are assigned. Dr. Gust testified that as a practical matter, due to lack of funding, the cutoff for funding is generally a score somewhere between one and two. Dr. Gust testified that in determining whether to provide marijuana, the Public Health Service peer review committee generally does not distinguish between proposals with lower scores and those with higher scores: "any project that has scientific merit is approved."[97] Indeed, according to Dr. Gust, "anything that gets approved gets NIDA marijuana. So it gets approved for NIDA marijuana with high enthusiasm, medium enthusiasm, or low enthusiasm. It doesn't matter, they're all approved to receive NIDA marijuana."[98] Dr. Gust also testified that he thought that a researcher seeking to obtain FDA approval to make whole-plant smoked marijuana into a prescription medicine would not have a problem obtaining marijuana from NIDA as long as the researcher had

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[96] *Id.*; Government exhibit 24, p. 3.
[97] Transcript p. 1,700.
[98] Transcript p. 1,701.

an IND from the FDA.

Asked on cross-examination about the Institute of Medicine statement that the purpose of clinical trials would not be to develop a licensed drug from smoked marijuana, Dr. Gust iterated his earlier statement that he thought that ultimately, any approved medication made from marijuana would be a purified constituent delivered in a non-smokable form. Nonetheless, according to Dr. Gust, there was not, in his experience, a bias against approving marijuana as medicine at the Public Health Service review level. However, Dr. Gust responded affirmatively when asked on cross-examination, "A privately funded researcher might well obtain the appropriate DEA Schedule I registration, have their protocol reviewed and approved by the FDA, and still be denied access to NIDA marijuana by a Public Health Service committee under the conditions and priorities that are set forth in this document; isn't that correct?"[99]

Dr. Gust further testified that as a general practice, the Public Health Service review committee did not disapprove any project, but would point out deficiencies and weaknesses to the researcher and deny approval until those deficiencies and weaknesses were corrected and a revised protocol was submitted. Dr. Gust testified that NIDA had approved "probably dozens"[100] of applications to receive marijuana for research in the ten years prior to the hearing.

Dr. Gust testified that there are only a "handful"[101] of Schedule I controlled substances available from commercial sources. Respondent subsequently introduced into evidence exhibits showing that thirty Schedule I substances are available from commercial sources; the Government asked me to take administrative notice that there are 125 Schedule I substances, which I did. The Government asserts that these exhibits do not impeach Dr. Gust's credibility.

D. MAPS' Decision to Seek Alternative Sources of Marijuana

1. Complaints About NIDA-Provided Marijuana

Dr. Doblin testified that the marijuana from NIDA had a low THC content, that using higher-potency marijuana would result in patients inhaling less particulate matter

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[99] Transcript p. 1,694.
[100] Transcript p. 1,740.
[101] Transcript p. 1,644.

for a given quantity of cannabinoids, and that he also wanted to experiment with strains of marijuana that contained other cannabinoids as well as THC. In addition, according to Dr. Doblin, some NIDA marijuana contained seeds, stems, and sticks; the presence of seeds meant that the female marijuana plants had not been separated from the male plants.[102] Dr. Doblin testified that female plants that have formed buds but that have not been allowed to go to seed are higher potency and that he thought that marijuana from such plants would be more likely to result in a satisfactory risk-benefit analysis from the FDA. Dr. Doblin further testified that the THC tends to be concentrated in the buds of the marijuana plant, and that leaves have lower concentrations of THC. Dr. Doblin testified that some of the NIDA marijuana was old, having been stored for years, and that it was also harsh.

In an article in the *Journal of Cannabis Therapeutics*, Ethan Russo, M.D., and his co-authors stated that patients complained that the NIDA-supplied marijuana was "harsh" or tasted "chemically treated."[103] The article further stated that the contents of the NIDA-supplied marijuana cigarettes were "a crude mixture of leaf with abundant stem and seed components . . . . The odor is green and herbal in character. The resultant smoke is thick, acrid, and pervasive."[104] The article concluded with a number of recommendations, including that "Improvement in a clinical cannabis program would include a ready and consistent supply of sterilized, potent, organically grown unfertilized female flowering top material, thoroughly cleaned of extraneous inert fibrous matter."[105]

Dr. ElSohly testified that he had seen this article, including a photograph in the article that showed debris in marijuana cigarettes. Dr. ElSohly testified that "there is no way that [the material shown in the photograph] is material that is actually in the

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[102] Dr. Voth, however, testified that he had "never seen anything systematic that said that seeds and stem constituents necessarily cause greater or less irritation."
[103] Ethan Russo, M.D., et al., *Chronic Cannabis Use in the Compassionate Investigational New Drug Program: An Examination of Benefits and Adverse Effects of Legal Clinical Cannabis*, 2(1) JOURNAL OF CANNABIS THERAPEUTICS 3, 48 (2002); Respondent exhibit 19. Dr. Doblin testified that there were four patients involved in the study.
[104] *Id.* at 49.
[105] *Id.* at 52.

cigarettes,"[106] because material of the size shown would have punctured the cigarette paper. Dr. ElSohly further testified that it was possible that some of the bulk material would look like that shown in the photograph.

Dr. Doblin testified that a Philip Alden, a patient who used marijuana in a NIDA study, complained to him about four years prior to the hearing in this matter that the marijuana provided by NIDA caused him to contract bronchitis and that his physician told him that the illness was due to the poor quality of the marijuana he had used, and that consequently Mr. Alden withdrew from the study. Dr. Doblin further testified that Mr. Alden told him that he had previously used a higher potency marijuana that he had obtained from buyers' clubs in California and that that marijuana use had improved his health. Dr. Doblin also testified that Mr. Alden declined to testify in this matter because he was concerned about the possibility that he would be prosecuted under federal law.

Dr. ElSohly testified that he had not received any complaints that the marijuana grown at the National Center had too many stems and/or seeds to be used for clinical research, but that Dr. Abrams had made comments to the effect that the marijuana had seeds in it. Dr. ElSohly further testified that from the inception of the marijuana growing program at the National Center, the growers had made an effort to remove seeds and other large particles from the plant material, but that the de-seeding machines they originally used made the material too fine to roll into cigarettes, and so RTI had said that it would be responsible for removing seeds from the material. Dr. ElSohly further testified that in 2001 the National Center worked with a company in Canada that designed a machine specifically to de-seed marijuana, and that the machine was put into operation that same year and removed seeds, stems, and any other heavy particles prior to shipping the marijuana material to RTI. Dr. ElSohly also observed that any large particles in the material would puncture the cigarette paper, and that the number of cigarettes that would have been subject to that problem even before 2001 would have been insignificant.

Dr. ElSohly testified that as of the date of the hearing, he had not received any formal complaints about the marijuana that the National Center provided. Dr. ElSohly testified that researchers from CMCR had requested marijuana at eight percent potency, and that he had offered to contact NIDA on their behalf and seek approval to make

[106] Transcript p. 1,306.

cigarettes at eight percent potency and that he had obtained the approval and made the cigarettes. Dr. ElSohly further testified that the cigarettes had turned out to have a potency above seven percent, that the variation between the actual potency and eight percent was not substantial enough to make a difference to the study, and that one of the researchers told him that he needed a batch of six percent potency because the seven-plus percent potency material was too strong for the subjects to tolerate.

Dr. Gust testified that he was not aware of any formal written complaints about the quality of NIDA-provided marijuana, nor had any researcher, doctor, or patient called him to advise him of any such complaints.

2. Other Concerns about NIDA Marijuana

Dr. Doblin testified that he had concluded that MAPS would need to obtain a source other than NIDA for marijuana, noting that NIDA is not in the business of supporting medical marijuana research and is not authorized by Congress to sell marijuana for prescription use. More specifically, Dr. Doblin testified that because MAPS seeks to obtain FDA approval for marijuana as a prescription medicine, it needs to establish a Drug Master File for a specific product and then conduct research on that product and have it available for marketing if it receives FDA approval. Dr. Doblin testified that MAPS would need a source of supply that would provide specific strains and quantities of marijuana whenever required, which NIDA does not do. Dr. Doblin further testified that although making a profit on a marijuana product is not MAPS' primary goal, it would need a reliable source of supply nonetheless and would also need to have control over the source of supply in order to meet FDA requirements. Dr. Doblin emphasized, in that connection, that the FDA requires the marketed drug to be the same one that was used in research. Dr. Doblin also noted that because NIDA marijuana is less potent than the marijuana that MAPS would like to use for research, the risk/benefit ratio of NIDA marijuana is less favorable, which would make it more difficult to secure FDA approval. In addition, Dr. Doblin testified, because Congress has not authorized NIDA to sell marijuana on a commercial basis, MAPS would have to negotiate with Dr. ElSohly, who would be a monopolist supplier and set whatever price he chose.[107]

[107] Dr. Doblin testified that he did not know whether Dr. ElSohly was precluded from supplying marijuana to anyone except pursuant to NIDA instructions.

IV. About Respondent and His Application for Registration

A. About Respondent

Respondent is a full professor in the Department of Plant, Soil, and Insect Sciences at the University of Massachusetts at Amherst. He received a Bachelor of Science degree in agronomy from the University of Wisconsin and in 1967 received a Ph.D. in the same subject from the University of Minnesota. Following active duty in the United States Army Chemical Corps, he was hired at the University of Massachusetts' University Experiment Station in Waltham, Massachusetts, where he worked from 1969 to 1976. Respondent then took a sabbatical leave in Cambridge, England, for six months and was hired at the Amherst campus on his return.

Respondent testified that he has done substantial work on the effect of air pollution on plant growth and development and that he also specializes in medicinal plants. Respondent testified that he receives funding for his research from, among other sources, the United States Environmental Protection Agency and the United States Department of Agriculture. Respondent testified that he is interested in growing marijuana for use in research trials because of his work with medicinal plants.

B. Respondent's Application for Registration as a Manufacturer of Marijuana

Dr. Doblin testified that once he concluded that MAPS would need its own source for marijuana, he concluded that inasmuch as Dr. ElSohly was affiliated with the University of Mississippi, a university affiliation would enhance the likelihood of obtaining DEA approval for registration as a manufacturer. Dr. Doblin further testified that he wanted someone with expertise in medicinal plants who was a tenured faculty member so that his or her career would not be jeopardized by involvement in a controversial issue and who would be able to resist pressure to withdraw the application. Finally, Dr. Doblin testified, he wanted someone who had not had any previous involvement in efforts to legalize marijuana. Dr. Doblin testified that he contacted various persons involved in botanical medicines and eventually someone recommended Respondent. Dr. Doblin testified that he telephoned Respondent and explained that MAPS focused on FDA-approved research rather than attempting to bypass the FDA via state initiatives, and that he would like to contract with Respondent to grow marijuana for

FDA- and DEA-approved projects. He told Respondent that MAPS would provide a grant to the university to cover the costs of growing marijuana if Respondent could obtain the requisite licensure. Dr. Doblin subsequently visited Respondent and discussed with him, among other things, the needs for various strains of marijuana, problems with obtaining marijuana from NIDA, and the risks of doing research with a drug that might not be available for prescription use. Dr. Doblin testified that he and Respondent also talked about MAPS' desire to operate like a standard pharmaceutical company and to obtain a supply of marijuana that it could take through the requisite testing process, as well as his decision to work on an alternative to smoking as a system to deliver marijuana.

Dr. Doblin testified that he and Respondent entered into a memorandum of understanding providing that MAPS would cover all costs associated with the project, that any equipment purchased would remain the property of the university if the contract ended, that MAPS would not claim any proprietary interest in any information that Respondent might obtain from the project, that MAPS would indicate where any marijuana Respondent grew would be used, and that the marijuana would only be used in government-approved studies.

Dr. Doblin testified that at this point he had stopped trying to develop marijuana research projects and was working on the vaporizer research and on obtaining an independent source of supply of marijuana. Dr. Doblin further testified that he knew that there was a pent-up demand for research on medical uses of marijuana, so that once he had a supply, it would not be difficult to develop appropriate projects.

Respondent testified that after his conversations with Dr. Doblin he spoke with various university officials, including his department head, his dean, personnel at the Office of Grants and Contracts, and the Vice Chancellor for Research, and that none of them had any objection. Respondent then submitted the appropriate internal university forms and, on June 25, 2001, an application for registration with the DEA.

Respondent testified that he had heard that marijuana was grown for research purposes, but that until Dr. Doblin contacted him he had no interest in cultivating marijuana himself. Respondent testified that several years earlier the state of Massachusetts had approached him about growing marijuana for medical uses and he had

done a little bit of research on the subject, and that after he talked to Dr. Doblin he researched the possibilities of marijuana "as perhaps a medicine that should be available to the public, not to violate security regulations or not to see it diverted into a recreational drug, but to – I thought it could be a medicine that could be used."[108]

Respondent testified that from his conversations with Dr. Doblin he understood that his role would be to produce marijuana and that MAPS would have direct contact with researchers and refer them to Respondent to obtain the marijuana they needed. Similarly, Respondent testified that his role with respect to research using vaporizers would be limited to supplying the marijuana used in testing the vaporizer.

Respondent testified that all research at the University of Massachusetts is done by source of funding, that he would not have filed the application to cultivate marijuana had Dr. Doblin not approached him, and that all the costs of growing marijuana, including the requisite expenditures for security, would have to be funded by a research grant to the university. Respondent also testified that at the time he filed his application, he had no idea how much marijuana the University of Mississippi produced and had only a minimal idea that there had been some complaints about the quality of the University of Mississippi's marijuana. Respondent testified that he became concerned about whether sufficient marijuana from the University of Mississippi was available to researchers.

Shortly after Respondent submitted the application, state investigators came to the university and discussed state security requirements, and also told Respondent that a state permit would depend upon obtaining federal registration.

C. Respondent's Process for Growing Marijuana

Respondent testified that he would grow marijuana much the same way he would grow other plants: he would grow plants from seed in a growing medium in a greenhouse, germinating the seeds in flats and then transferring the seedlings to pots. Respondent said that he would probably prefer to obtain seeds from an outside source rather than collecting seeds from the plants he grew, but that he would follow DEA instructions on the matter. Respondent testified that he had a room available that had one wall in the earth and only one door, as required.

Respondent testified that he would have to purchase a drying oven because those

[108] Transcript p. 212.

that he had were too large and could not be secured. Respondent testified that it would be possible to grow marijuana in a completely controlled environment, thereby making it possible to obtain more information about optimal conditions for growing the plant for various purposes, but whether he could construct that environment would depend on his funding.

D. How the Marijuana Respondent Proposes to Grow Would Be Utilized

Respondent testified that as a non-profit institution the University of Massachusetts would not make any profit on the marijuana he would grow, and that he had not sorted out the details as to how much researchers would have to pay for marijuana he supplied to them.

Respondent testified that he did not know who the potential customers for his marijuana would be and that MAPS might direct researchers to him, but that in any case those researchers would be properly licensed. Respondent testified that he knew that MAPS planned to sponsor research using a vaporizer device to deliver marijuana without burning it, but that he did not know who would develop the device, whether the company was currently permitted to receive marijuana for research, or what quantity or quality of marijuana the company would need.

Dr. Doblin testified that if Respondent's application is approved, Respondent will manufacture marijuana according to MAPS' requests for certain potencies, that Respondent would provide it to researchers at MAPS' direction, and that MAPS would allocate the marijuana first to projects it sponsored and then, if sufficient marijuana was available, to other researchers either for free or at cost. Dr. Doblin emphasized that MAPS would at no time have possession of any marijuana.

Dr. Doblin testified that if Respondent's application is approved, MAPS intends to develop a clinical plan in consultation with the FDA, which will include the selected patient population, the sequence of studies to be conducted, and the time frame for those studies. He said that MAPS would then solicit researchers to conduct the studies.

Respondent testified that if he becomes registered, he has no intention of replacing NIDA as a supplier of marijuana for research, but only to provide an alternative supplier. Respondent also testified that he would pursue the application even if he knew that the National Center supplied an adequate quality and quantity of marijuana to

researchers, because under the current arrangement the government decides what research is relevant and because an alternative source of supply would be appropriate for comparison purposes.

E. The DEA's Actions With Respect to Respondent's Application

1. Initial Activity

Respondent testified that eight or nine months after submitting his application, he still had not heard from the DEA, so he contacted the agency and eventually was referred to Diversion Investigator Sharon Lick, who advised that the DEA had not received Respondent's application and that he should file it again. Subsequently, however, Respondent received the June 25, 2001 application back from the DEA; it was date stamped June 28, 2001. Respondent again called Investigator Lick and told her that the application had been returned to him. According to Respondent, Investigator Lick then told him that he filled out the application incorrectly and should submit a new one, but when he went through the form with her, she had no corrections to make.

On August 22, 2002, Respondent resubmitted his application, along with written responses to various questions that Investigator Lick had sent him. Specifically, Respondent stated, among other things, that the purpose of applying for a registration to manufacture marijuana was to supply a defined (i.e., grown to specifications) marijuana product to investigators undertaking clinical trials with marijuana; that MAPS would provide the funding for the work; that the research would involve either smoked marijuana or marijuana delivered by a vaporizer device; that the marijuana would be grown in a secure and environmentally controlled room; and that Respondent estimated that about twenty-five pounds of marijuana (dry weight) would be grown in the first year with a THC level of seven to fifteen percent. Respondent testified that Dr. Doblin assisted him in preparing answers to these questions.

Although in responding to the questions Investigator Lick sent him Respondent referred to smoked marijuana, he testified that the only proposed use of which he was aware for the marijuana he sought to grow is vaporizer studies, and that he would need the authority to grow marijuana to be smoked in order to allow for comparisons between smoked and non-smoked material. Respondent testified that he probably referred to smoked marijuana because smoking is a common delivery system for the drug, but that as

of the date of the hearing and because he had read more about smoked marijuana, he found that a "less attractive delivery means."[109] Respondent further testified that if he produced marijuana for use by researchers who utilized it in smoked form, he would provide it in bulk, not rolled into cigarettes.

Respondent testified that about six to eight weeks after he submitted the August 2002 application, two DEA investigators visited the campus and met with Respondent, his department head, the dean, and the Vice Chancellor for Research. Respondent testified that he thought the DEA personnel were trying to discourage the university from undertaking the project, but that the university officials said that the university was a research institution and that "these are the type of problems that we worked on."[110]

Respondent testified that DEA personnel made a second visit to the university in either the fall of 2003 or the spring of 2004, and that during this visit they walked around the campus with him and discussed where and how the marijuana would be grown. Respondent testified that the DEA personnel thought the room he proposed to use to grow marijuana could be made secure and that he also showed them a room which would be connected to the growth room and where he would dry the material.

In a letter dated June 2, 2003, to Frank Sapienza, then Chief of the Drug and Chemical Evaluation Section of the DEA's Office of Diversion Control, Respondent stated that testing marijuana for medical use would cost several million dollars, an expense that private drug companies would be hesitant to incur unless they were assured that they would be able to evaluate various sources for marijuana. Respondent testified that he based this statement on anecdotal evidence of the cost of developing new drugs, but that he had not received any specific information on the subject from any pharmaceutical company. Respondent also stated in the letter that in private conversations, researchers had indicated to him that they were afraid they would lose their access to marijuana if they complained about the material currently available to them. Respondent testified that he based this statement on conversations with Dr. Doblin, on conversations at a conference he had attended, and from emails from various individuals, but that he did not know if these emails were from legitimate researchers and

[109] Transcript p. 241.
[110] Transcript p. 43.

did not have any information about whether any legitimate researchers had stated their complaints to NIDA.

Respondent attached to the letter a copy of an article dated January 24, 2003, from the *San Mateo Times* and a copy of a letter dated March 11, 2003, from Dr. Russo, the neurologist with whom MAPS had been working, to Mr. Sapienza. The newspaper article stated that doctors conducting a study to discover whether marijuana cigarettes could be safely provided to HIV/AIDS and cancer patients to treat symptoms and side effects of the treatment of their diseases "want better quality weed from the federal government."[111] The article quoted Dennis Israelski, M.D., as saying that "[t]he study continues, but is going slowly for a variety of factors,"[112] and also advised that "some believe the apparently low-grade marijuana used in the program – grown at the University of Mississippi by the federal government – has discouraged participants who can treat themselves with the drug through other channels. And stringent physical requirements on often terminally ill patients have also slowed membership in the study."[113] The article also stated that Phillip Alden (about whom Dr. Doblin testified, as noted above) dropped out of the study when he contracted bronchitis, and quoted Mr. Alden as stating that he would rejoin the research if the quality of the marijuana improved and that he believed the papers in which the cigarettes were rolled contained toxins.

The letter from Dr. Russo stated, among other thing, that he had held Schedule I registration since 1996 and possessed 100 grams of NIDA marijuana since 1997, but that "the material was of such poor quality, we did not deem it to be representative of true medical cannabis, and have not yet ascertained an appropriate set of biochemical experiments for which to utilize it."[114] Dr. Russo further stated that the only reason he had not completed his clinical study of cannabis in migraine was that NIDA had refused to supply the material, that the reason the University of Massachusetts facility was necessary is that "all FDA-worthy studies should have access to clinical cannabis without

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[111] Jean Whitney, *Doctors Want Better Marijuana for Study*, SAN MATEO TIMES, Jan. 24, 2003; Government exhibit 30a.
[112] *Id.*
[113] *Id.*
[114] Letter from Ethan Russo, M.D., to Frank Sapienza (March 11, 2003); Government exhibit 30b, p. 1.

superfluous, expensive, and redundant Public Health Service oversight,"[115] and that he was taking over another researcher's compassionate use IND because NIDA had not responded to that researcher's request for higher-potency material. Dr. Russo stated that he admired Dr. ElSohly and his colleagues and harbored no personal animus against them, and that he had not said NIDA was incapable of producing quality marijuana, but that "[d]espite protestations to the contrary, NIDA continues to supply seeded material that is poorly cured, and relatively impotent."[116] Dr. Russo further stated that in light of the cost of Phase III clinical trials, "no sponsor of cannabis research is likely to accept a situation in which they have no control over the product that they hope to be marketing in the future."[117] Dr. Russo closed his letter by stating that "it is grossly evident that NIDA is profoundly conflicted in serving as purveyor of cannabis for medical studies, and there is no better reason that the University of Massachusetts should advance with the project."[118]

Respondent testified that he received a notice by mail inviting him to bid on the contract to grow marijuana for NIDA, but concluded that there was little likelihood that he could put forward a successful bid in light of the University of Massachusetts' lack of experience in growing marijuana. Respondent also testified that he was not interested in analyzing seized material, which would be required by the contract, although he had the instruments to do that work.

2. Dr. ElSohly's Comments and Objections to Respondent's Application

Dr. ElSohly testified that the DEA sent him the *Federal Register* notice of Respondent's application,[119] and that he filed comments and objections to that application in a letter dated September 9, 2003. In the letter, Dr. ElSohly stated, among other things, that the University of Mississippi provided its subcontractor with marijuana that had

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[115] *Id.*
[116] *Id.*
[117] *Id.*
[118] *Id.*; Government exhibit 30b, p. 2.
[119] The DEA's regulations, at 21 C.F.R. § 1301.33, require the agency to mail copies of the *Federal Register* notices of applications for registration to bulk manufacture a Schedule I or II controlled substance to all persons who are currently registered or have applied for registration to manufacture that basic class of substance.

"absolutely no seeds or heavy stem particles,"[120] that the University of Mississippi had not received any formal complaints about the adequacy of the marijuana it provided for research, and that "we strongly feel that it is absolutely unnecessary to approve another manufacturer's registration to manufacture (cultivate) marijuana and tetrahydrocannabinols for distribution to approved researchers. Approval of the University of Massachusetts-Amherst [application] would result in a duplication of existing resources without any foreseeable benefits."[121] Dr. ElSohly testified that he meant by this statement that the "duplication of efforts in terms of production of marijuana for research and distribution of that marijuana for research is a duplication of effort where there is no deficiency to be covered at this time as far as I can see, and so there is no benefits other than you just have another producer."[122]

In a draft of his comments that he had sent to Dr. Gust on August 29, 2003, Dr. ElSohly stated, "Those researchers with projects that do not meet the scientific approval criteria by NIDA would not receive marijuana free of charge. Rather, if those researchers wish to carry out their research project(s), they are nonetheless still allowed to receive their needs of marijuana but they are required to pay for the material (the cost of production has been calculated and the researchers would pay just the production costs),"[123] and that "In addition to the above-described NIDA program and the availability of materials through that program, we at the University of Mississippi have a separate DEA registration . . . to manufacture (cultivate) marijuana and manufacture tetrahydrocannabinols. Materials could be made available to researchers that are properly registered with the DEA and that for some reason do not want or choose to go through the NIDA program or somehow do not qualify to receive materials under the NIDA program. We are prepared to meet any need, qualitatively and quantitatively, in this area."[124] These statements do not appear in Dr. ElSohly's comments as submitted to the DEA, and on cross-examination Dr. ElSohly testified that he should not have included

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[120] Letter from Mahmoud A. ElSohly, Ph.D., to the Deputy Assistant Administrator, Office of Diversion Control, DEA (September 9, 2003); Government exhibit 5, p. 3.
[121] *Id.*
[122] Transcript p. 1,423.
[123] Draft of *Federal Register* comments attached to an email from Dr. ElSohly to Dr. Gust on August 29, 2003; Respondent exhibit 5.

these statements and that he knew he could not provide plant material except through NIDA.

Dr. Gust testified that he commented on Dr. ElSohly's response to Respondent's application, but that his review was primarily for factual accuracy.

3. The DEA's Investigation Pertaining to Respondent's Application

Matthew Strait, Unit Chief for the Quota and U.N. Reporting Unit, Drug and Chemical Evaluation Section, of the DEA's Office of Diversion Control,[125] testified that when the Office of Diversion Control receives an application for registration to bulk manufacture a Schedule I or II controlled substance, the application is sent to the Registration Unit, which assigns a control number to the application and forwards it to the appropriate section of the agency (as of September 2004, Mr. Strait's office) for further action. Mr. Strait further testified that according to the normal practice in 2001, Respondent's application would have been assigned to a diversion investigator.

Mr. Strait testified that Respondent's application did not come to his attention until October 2002 and that he thought that the delay was due to the then-Administrator's criticism of the Office of Diversion Control for not informing the Administrator's office about registrations of certain researchers to work with marijuana and a consequent "virtual paralysis when anything came out with regard to marijuana."[126] Mr. Strait further testified that Respondent's application was filled out incorrectly because although Respondent listed the drug code number for marijuana, he failed to circle it, as required by the application's instructions.[127] Mr. Strait further testified, however, that he did not discuss this point with Investigator Lick, who apparently was then the diversion investigator in charge of the DEA's Registration Unit, and that he did not know whether

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[124] *Id.*

[125] The Office of Diversion Control is a component of DEA's Division of Operations and consists of sections which are further divided into units.

[126] Transcript p. 923.

[127] The drug code numbers are handwritten on Respondent's application. The application form states, in item 8, that applicants for registration to manufacture substances in "Schedule I, II, III, IIIN in addition to codes furnished, . . . MUST Circle Below those 'Basic Classes' of controlled substances in Schedule I and II which you propose to 'Manufacture in Bulk'[.]" [Emphasis in original.] Mr. Strait testified that "I know it seems like a [moot] point, but if they [applicants] don't circle it, it has a vastly different way that it's processed within the office." Transcript p. 929.

this defect contributed to the delay in processing the application. Mr. Strait testified that Respondent's application raised other issues as well, notably that Respondent sought to manufacture a Schedule I substance in order to develop a pharmaceutical product; the right of the University of Mississippi to comment on the application, which might result in a hearing; and the DEA's longstanding concerns about MAPS and Dr. Doblin.

On March 4, 2003, Mr. Sapienza wrote to Respondent, advising that it appeared that the basis for Respondent's application was an alleged need for more potent and higher quality marijuana and that the DEA had legal and international treaty concerns about the application. Mr. Sapienza wrote that the DEA also disagreed with Respondent's assessment of the availability of marijuana to the research community because the agency had contacted NIDA, the Department of Health and Human Services, and various researchers and had concluded that the quantity and quality of marijuana available from NIDA was acceptable. The letter further stated that the DEA had received a copy of Dr. Russo's letter, that Dr. Russo was not registered by the DEA to conduct research with marijuana, and that the agency was not persuaded by Dr. Russo's arguments. Mr. Sapienza closed by asking Respondent to provide any credible evidence of his assessment of the issue and especially any correspondence with NIDA on the matter.

a. The Interviews of Researchers

On September 23, 2003, Mr. Strait and Diversion Investigators Lydia Bagley and Lucia Bartolomeo met in San Diego, California, with staff members of the CMCR and researchers working under CMCR auspices. Mr. Strait testified that he opened the meeting by explaining that he was there because the DEA had received an application for registration to cultivate marijuana, that the application had raised issues about the quality and potency of the National Center marijuana, and that the DEA wanted to know the researchers' thoughts on these issues. Dr. Igor Grant, head of CMCR, provided an overview of CMCR and its three-stage research mission: (1) look at the effect of smoked marijuana in certain patient populations; (2) identify novel drug delivery systems, such as inhalants, sprays, and vaporizer devices; and (3) research the constituent cannabinoids or slightly altered forms of them, to see if they could be used in certain populations. Mr. Strait testified that at the time of his meeting with CMCR personnel, the research was in the first of the three stages.

Mr. Strait gave the researchers a questionnaire, which the participants discussed at the September 23 meeting; Heather Bentley, a CMCR staff member, then wrote in additional comments and returned the questionnaire to Mr. Strait about two-and-a-half months later. The questionnaire asked whether CMCR was responsible for coordinating with NIDA to obtain marijuana; what the process was for obtaining marijuana; what forms and strengths of marijuana CMCR used; who placed the request for the drug; how the order was placed; how CMCR determined how much marijuana its researchers needed; how the marijuana was shipped; what security measures were in place during shipment; how much time elapsed between placing the order and shipment; whether CMCR was billed for the material; the cost of each cigarette; how the cost of marijuana compared to other potentially efficacious substances used in research; how the cigarettes were stored; what security measures were in place; whether ample stocks were available; how the cigarettes were dispensed to patients; whether any patients had encountered problems obtaining the marijuana cigarettes they were prescribed; whether any problems in obtaining marijuana had compromised the study; whether the method by which CMCR received marijuana cigarettes from NIDA was adequate; what CMCR's future research interests were with respect to marijuana; whether CMCR had any information that marijuana would be unavailable through NIDA in the future or that the supply would be insufficient; whether CMCR had had any difficulty in obtaining marijuana from NIDA in all the requisite strengths; whether such difficulties had been documented, whether they threatened the integrity of the research protocol, and how the issue had been resolved; whether NIDA had ever refused to supply marijuana to CMCR researchers with approved protocols; whether, based on its anticipated future research needs, CMCR had any concerns about the availability of research-grade marijuana from NIDA; whether the person responding to the questionnaire had visually inspected the cigarettes received from NIDA and whether there was a visual difference between the placebo and the non-placebo product; whether there was a visual difference among the cigarettes containing different levels of THC; whether the potency of the current product was consistent; whether the person responding had observed any physical deformities in the cigarettes' appearance; what plant parts had been observed in the cigarettes; whether the presence of plant parts rendered any of the cigarettes unacceptable for research; whether any patients

had complained about the harshness of the material; whether any issues of quality of the material had adversely affected the research; the potency of the marijuana currently approved for research; whether the current product was adequately potent; whether information received from any of the ongoing studies indicated that the potency of the marijuana was inadequate; whether the responder had sought a higher-potency product; whether it would be clinically important to evaluate the efficacy of a higher-potency cigarette; whether any information suggested that a higher-potency product would have a beneficial outcome compared to the product NIDA currently provided and, if so, whether the benefits would outweigh the risks; what alternative potency could be safely administered; what safety concerns would be associated with a higher-potency product; and whether CMCR had contacted NIDA to ascertain whether producing a higher-potency product would be feasible.

At the meeting, Dr. Grant said that visual examination of both the placebo and non-placebo NIDA marijuana disclosed no differences between them; and that he had visited the University of Mississippi growing operation and was satisfied with the consistency of its product. He added that the product was mostly devoid of seeds and stems, but that there was some variation within a range of potency. Dr. Grant told Mr. Strait that the marijuana from the National Center was sometimes harsh and caused patients to cough, but that nothing in the quality of the product affected CMCR's research. Ms. Bentley subsequently added to CMCR's responses to the questionnaire a comment that the researchers would prefer that the strength of the marijuana in the cigarettes they received from the National Center be more consistent. Mr. Strait further testified that Dr. Grant told him that the National Center guaranteed the potency of its marijuana within a specified range and that pursuant to discussions with NIDA, CMCR had concluded that a potency of eight percent was appropriate.

Also on September 23, 2003, Mr. Strait telephonically interviewed Ronald Ellis, M.D., Ph.D. The questionnaire that Mr. Strait prepared for Dr. Ellis and other researchers differed from that he gave to the CMCR personnel; the questionnaire Mr. Strait gave to Dr. Ellis asked, in substance: whether patients had experienced problems obtaining marijuana cigarettes they were prescribed for research; whether the method by which the researcher received marijuana from NIDA was adequate; what future research interests

the responder had that would require using marijuana; whether the responder had any information indicating that the supply of marijuana from NIDA would be insufficient in the future; whether the researcher had visually examined the NIDA marijuana and, if so, whether there were any visible differences between the placebo and non-placebo product or among products with varying levels of THC; whether the potency of the current product was consistent; what plant parts the researcher had observed in the product; whether any of the plant parts in the product rendered it unacceptable for research; whether patients had complained about the "freshness" of the marijuana; whether issues concerning the quality of the marijuana had adversely affected the research; what the potency was of the marijuana used in the responder's research; whether the potency of the product was adequate for the research; whether the researcher had sought a higher-potency product; whether it would be clinically important to evaluate the efficacy of a higher-potency product for the researcher's patient population and, if so, what would be the benefits and risks, whether the former would outweigh the latter; what alternative potency could be safely administered to the patient population; and what would be the safety concerns.

Dr. Ellis said, in substance, that his patients had not had problems obtaining marijuana he prescribed to them; that the method by which he obtained marijuana from NIDA was adequate; that he had no information indicating that the supply of marijuana in the future would be insufficient; that he had not visually examined the cigarettes supplied to his patients; that there had been some variation in at least two marijuana shipments between the stated and the measured potency, and "they have been very responsive";[128] that some patients had reported the smoke was harsh and they found it difficult to finish the cigarette, but this had not adversely affected the research, although one patient had dropped out of the study because he developed a cough related to the harshness of the marijuana; and that although marijuana that was supposed to be a potency of eight percent had tested as seven percent, this potency was adequate and potency was not a limiting consideration in his research.

Dr. ElSohly testified that he thought that the notation about the variability between the stated and the analyzed THC content referred to the batch of cigarettes,

described above, that was supposed to be at eight percent potency and that was analyzed at seven-plus percent potency. Dr. ElSohly further testified that he never received any formal complaints about the harshness of the cigarettes that the National Center provided, but he did hear unofficially about harshness, particularly attributed to the placebo material, and that he thought this harshness would be due to the nature of placebo material: all the components had been extracted out.

Also on September 23, 2003, Mr. Strait interviewed Jody Cory-Bloom, M.D., Ph.D., in person. Dr. Cory-Bloom said that patients had not had any problems obtaining the marijuana prescribed to them; that the method for obtaining marijuana from NIDA was adequate; that she was interested in research into delivering marijuana by means other than smoking; that she had not observed any visual difference between the placebo and non-placebo products; that she used marijuana of four percent potency, did not need a higher potency for her current study but would be interested in using higher concentrations perhaps in future work, and did not know whether the potency of the product she received was consistent, apparently because she was a blinded investigator, i.e., she did not know what the research subjects received; that a patient had complained to her that the product he had used was harsh, but she did not know whether he had used marijuana or the placebo; and that she found it difficult to recruit patients to participate in studies using smoked marijuana because people were not smoking marijuana as much as they used to, there were many criteria for inclusion in the study, and a time commitment was required.

Dr. ElSohly testified that he had not received this complaint about harshness, and that it may have been the case that the patient in question was being administered placebo material.

Also on September 23, 2003, Mr. Strait telephonically interviewed Dennis Israelski, M.D. Dr. Israelski said that his patients had not had problems obtaining the marijuana he prescribed; the method for obtaining marijuana from NIDA was adequate; he had no reason to believe that the supply from NIDA would be insufficient in the future; the potency of the product he had received was consistent; he had not observed any physical deformities in the product; he did not recall any complaints from patients

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[128] Government exhibit 17, p. 6.

about the freshness of the marijuana; and that the potency of the product he received was adequate for his research. Dr. Israelski also discussed the *San Mateo Times* article that Respondent had sent to the DEA, and denied making comments to the newspaper about the quality of the marijuana he obtained from the National Center. Indeed, according to Mr. Strait, Dr. Israelski said he had stopped reading that newspaper and was very upset because the article misrepresented him. Mr. Strait testified that with respect to Mr. Alden's comments in the article, Dr. Israelski said that subjects' perceptions of quality sometimes differ from that of the researcher, and that he wished he had prescreened Mr. Alden's comments to the reporter.

On September 24, 2003, Mr. Strait interviewed Mark Wallace, M.D., by telephone. Dr. Wallace said that his patients had not had difficulty obtaining the marijuana he prescribed for them; the method by which he received marijuana from NIDA was adequate; he did not have information indicating that the supply of marijuana from NIDA would be insufficient in the future; he was a blinded researcher and therefore would not have been in a position to distinguish active material from placebo; he could not comment on whether the potency of the product was consistent; patients had not complained about the freshness of the marijuana; and that the potency of the product he received was adequate but that future studies could look at higher potencies, which would have less tar and other components found in smoke.

That same day, Mr. Strait interviewed John Pollich, Ph.D., of the Scripps Research Institute. Dr. Pollich said he had not had any difficulty obtaining marijuana from NIDA; the method by which he received marijuana from NIDA was adequate; he had no information to indicate that a sufficient supply of material would not be available from NIDA in the future; there was no visible difference between the placebo and the non-placebo material; the potency of the material was consistent and adequate; he was very impressed and pleased with the material and had not seen any seeds or stems in it; plant parts would have made the material unacceptable for his research; of more than 100 subjects, no more than three might have complained that the product was harsh; the quality of the material did not adversely affect his research; and the product was adequate for his research.

On September 29, 2003, Mr. Strait telephonically interviewed Dr. Abrams, the

researcher on AIDS about whom Dr. Doblin testified. Dr. Abrams said that his subjects were all in an inpatient setting and had no difficulty obtaining the marijuana he prescribed to them; the method by which he received marijuana from NIDA was adequate; he would in the future like to do research on marijuana using a vaporizer protocol and on comparing cannabis with standard anti-nausea drugs in cancer patients; he had no information indicating that the future supply of marijuana from NIDA would be insufficient; he had visually inspected the marijuana from NIDA and had seen no difference between the placebo and non-placebo material; the cigarettes were nicely rolled, but some material spilled out of the ends; he had observed seeds, leaf, and some stems in the product, which made the potency inconsistent and adversely affected his research because the material did not mimic that which was available in the San Francisco area and because he was trying to minimize the harmful components resulting from smoke while optimizing the medical value of the THC; the harshness of the product caused a cough that was different from the cough generally caused by smoking marijuana; about four of the fifty patients in his studies had left because of the harshness of the marijuana; he wanted to conduct research with a higher-potency marijuana that would be more similar to what was available on the street but the Scientific Review Board of the University of California at San Diego, which would have to approve his study, and CMCR, which funded his work, had raised questions about doing so; and he thought that using a higher-potency product would enable his patients to obtain a pharmacologic effect from consuming a smaller quantity of material.

Dr. ElSohly testified that Dr. Abrams had mentioned the issue of harshness in passing when Dr. Abrams and Dr. ElSohly were walking with a group at an International Cannabis Research Society meeting, but had not asked him to take any action and that there was nothing he could have done about it. Dr. ElSohly also testified that it is to be expected that some material would fall out of the cigarettes. Dr. ElSohly testified that the cigarettes are placed vertically in cans, 300 cigarettes per can, and that the tops and bottoms of the cigarettes are open because that is how the rolling machine makes them. Dr. ElSohly further testified that he did not think it made any sense to try to match the potency of marijuana found in any one geographical area, but rather to consider national potency data. Dr. ElSohly also emphasized that in clinical trials the subjects must smoke

the entire cigarette, not merely a portion of it, and that it would be irresponsible to provide subjects with material whose potency was above average.

With respect to the comment that two or three subjects dropped out of the study because of the harshness of the NIDA-provided marijuana, Dr. ElSohly testified that it was not known whether these subjects used the placebo or the active material and that even if four of the fifty patients dropped out, ninety-two percent of the subjects completed the study, which was a good outcome.

Also in September 2003, Mr. Strait visited two facilities in La Jolla, California, where researchers from the University of California at San Diego were conducting studies using marijuana.

On December 18, 2003, Mr. Strait interviewed Aaron Lichtman, Ph.D., of Virginia Commonwealth University. Dr. Lichtman said he had not had any problems obtaining marijuana from NIDA; the method by which he received marijuana from NIDA was adequate; he had no information indicating the supply from NIDA would be insufficient in the future; he obtained bulk marijuana and observed that the active material was sticky, while the placebo was not, the placebo burned more quickly, and there was a slight difference in smell between the two; the potency of the material he received was consistent; he had observed leaves, seeds, buds, and twigs in the material, which he removed and which did not adversely affect his research; he would prefer higher-potency material, but as of the last time he had received product, in approximately 1999, the highest potency available was three to four percent; and he had not checked recently to see if a higher-potency product was available.

Mr. Strait testified that he believed that he contacted all the researchers who were working on studies of marijuana as medicine, but that he did not contact the patients using NIDA-supplied marijuana in compassionate use programs because they were not researchers.

b. The Meetings with Other Agencies

In October 2003, Mr. Strait visited RTI and in December of that year he visited the University of Mississippi. In mid-January 2004, Mr. Strait and other DEA personnel met with representatives of NIDA, including Dr. Gust, to discuss NIDA's marijuana cultivation program and its contract with the National Center. Mr. Strait testified that in

December 2003 he also met with Mr. Egertson of the Department of Health and Human Services to talk about the Public Health Service process and that during the meeting with Mr. Egertson, he also spoke via conference call with FDA personnel.

Dr. Gust testified that he met with representatives of the DEA in January 2004 and discussed Respondent's application, but that he had little recollection of the meeting other than that it occurred. Dr. Gust testified that he thought the meeting was essentially for the DEA to provide NIDA with information about the application, and that although he did not recall ever having been asked to participate in a meeting about an application for DEA registration to manufacture a controlled substance before, he did meet with DEA representatives on a variety of topics. Dr. Gust testified that NIDA did not oppose Respondent's application and that although there was discussion within NIDA about whether to respond to the *Federal Register* notice of Respondent's application, NIDA's director or deputy director decided that NIDA would not submit a response.

c. Further Developments

Respondent testified that the DEA published a notice of his application in July 2003, but that he heard nothing more from the agency so he filed a lawsuit in December 2004. Apparently, MAPS also sued NIDA over its failure to make a decision on the Chemic application. Dr. Doblin testified that the United States Circuit Court of Appeals for the District of Columbia Circuit asked the DEA to explain why it had not acted on Respondent's application and dismissed the case against NIDA.

Mr. Strait testified that in the fall of 2004 he attended another meeting of DEA personnel to discuss Respondent's application. As a result of that meeting, the then-Deputy Assistant Administrator for the Office of Diversion Control directed Mr. Strait and Diversion Investigator Helen Kaupang to draft a decision paper for the Deputy Administrator to enable her to provide guidance as to how to proceed on Respondent's application. On December 10, 2004, the then-Deputy Assistant Administrator of DEA's Office of Diversion Control issued the Order to Show Cause that gave rise to this proceeding.

Respondent testified that he considered the allegations in the Order to Show

Cause pertaining to smoked marijuana "curious"[129] because he had made it clear in his application for registration that he intended to cultivate marijuana for research using a vaporizer, not smoked marijuana. Respondent further testified, with respect to the statements in the Order to Show Cause about New Drug Applications, that there was nothing in the application materials suggesting that an NDA was a prerequisite for a manufacturing registration.

V. Other Evidence

A. Evidence About Commercial Use of Marijuana Outside the United States

An English company, GW Pharma Ltd., produces Sativex, which contains extracts of THC and cannabidiol in an oral spray and is used to treat neuropathic pain in patients with multiple sclerosis. It is marketed in Canada but not in the United States. Dr. Doblin testified that GW Pharma, Ltd., obtained permission from the Home Office to grow marijuana that it uses to produce extracts and a sublingual spray, and that the company is seeking approval for its products in England, and plans to try to obtain approval in the United States.

In the United Kingdom the National Cannabis Agency, an office within the Home Office's Drugs Branch, is the government agency responsible for regulating marijuana pursuant to the Single Convention. According to a protocol in effect since April 1, 2005, premises licensed to produce, possess, or supply marijuana are designated as sites of the National Cannabis Agency, and when marijuana is cultivated at licensed sites "a form of constructive purchase and possession will be deemed to have taken place between the [National Cannabis] Agency and producer with actual ownership and possession of the material reverting immediately to the producer for the purposes for which the license was granted . . . ."[130] The protocol further provides that "any import, export or wholesale dealing from a licensed [National Cannabis] Agency site will be deemed to have taken place with the explicit authority of the [National Cannabis] Agency"[131] and that marijuana on a producer's premises is to be treated as stock held constructively by the

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[129] Transcript p. 53.
[130] United Kingdom National Cannabis Agency: Protocol, paragraph 6(b); Respondent exhibit 26, p. 2.
[131] United Kingdom National Cannabis Agency: Protocol, paragraph 6(c); Respondent

National Cannabis Agency unless at the point of cultivation the producer designates it for distribution to third parties, in which case it is to be separately identified on the producer's premises.

B. Other Support for Respondent's Application

Dr. Doblin testified that Respondent had told him that he had been contacted by the state of Massachusetts some years earlier about growing marijuana for the state's medical marijuana program, but that the state had not had any funds for such a project. Dr. Doblin testified that consequently, it was deemed necessary to obtain support for Respondent's application from members of the Massachusetts delegation in Congress.[132]

By letter dated June 6, 2002, Representatives Barney Frank, John Olver, James McGovern, William Delahunt, and Michael Capuano wrote to the then-Administrator of the DEA to support registering private funded sources of marijuana for use in federally approved studies. In a response dated July 1, 2002, the then-Administrator noted, among other things, that:

> The Single Convention requires any party that permits the cultivation of marijuana for scientific purposes to ensure that such cultivation occurs only under the oversight of a national government agency, with the agency maintaining a monopoly over the distribution of all marijuana grown for research. Cultivation of marijuana by private growers not under the oversight of a national agency is prohibited by the treaty, as is distribution of marijuana by private entities. These requirements are necessary to minimize the likelihood that marijuana grown for research will be stolen or diverted into illicit channels, or that individuals will use their authority to cultivate for research as a subterfuge for illicit production and distribution. Such concerns are particularly heightened in the United States, where marijuana is the most widely used illegal drug.[133]

The Administrator further stated that:

> Both the Single Convention and the [Controlled Substances Act] contemplate that domestic production of marijuana for scientific purposes must be limited to the minimum number of establishments that can produce an adequate supply. For more than 30 years, the University of Mississippi has produced an adequate supply to meet the entire United States demand for research-grade marijuana. There is no indication that this supply is currently inadequate or will become

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exhibit 26, p. 2.

[132] Dr. Doblin testified that "we felt it was necessary," but did not provide an antecedent for the pronoun. Transcript p. 585.

[133] Letter from Asa Hutchinson, Administrator, DEA, to John Olver, Member, United States House of Representatives (July 1, 2002); Government exhibit 55, p. 1.

> inadequate in the future. As long as the University continues to meet the nation's needs for research-grade marijuana while maintaining the highest level of safeguards against diversion, the Single Convention and the [Controlled Substances Act] dictate that it remain the sole domestic producer.[134]

By letter dated October 20, 2003, United States Senators Edward Kennedy and John Kerry expressed support for Respondent's application. By letter dated July 26, 2005, various members of the House of Representatives from Massachusetts also expressed their support for Respondent's application.

C. Other Evidence Pertaining to the Statutory Factors

Respondent testified that he intends to comply with all applicable state and local laws if his DEA application is granted, and that he would not make any marijuana he grew available to anyone other than researchers who have the appropriate federal approval to use it.

With respect to technical advances in the art of manufacturing controlled substances, Respondent testified that he thought that by being able to supply marijuana to investigators he would advance the understanding of any potential clinical use for it, and that he also would learn more about how the environment in which marijuana is grown would affect the plant's constituents. Respondent testified that the purpose of manufacturing marijuana would be to test various delivery systems and determine whether they would be effective.

Respondent testified that he did not hold any patents with respect to medicinal plants.

With respect to his conviction record, Respondent testified that he once received a speeding ticket, and has never been convicted of anything else.

Respondent testified that he had never grown marijuana or any other controlled substance and thus had no experience in controlling against diversion, but that he had been working closely with the DEA personnel who visited his facility to establish appropriate conditions, that he had agreed to their requirements, and that the university understood the need for appropriate security. Respondent also testified that as far as he knew, only the one current registered manufacturer of marijuana has experience in its licit

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[134] *Id.*; Government exhibit 55, p. 2.

cultivation.

Finally, Respondent testified that as a scientist he seeks to advance the inquiry into whether marijuana can be used clinically.

Dr. ElSohly testified that a cultivator of marijuana that did not want to perform analysis of samples provided by the DEA required by the National Center's contract with NIDA could subcontract that portion of the contract.

THE PARTIES' CONTENTIONS

The Government asserts, in substance, with respect to the statutory factors, that (1) Respondent has not shown that the marijuana distributed by the National Center is of insufficient quality and potency, and even if there were problems with this product, Respondent has not offered any evidence as to what he would do about it; (2) the Administrator has discretion pursuant to 21 C.F.R. § 1301.33(b) to limit the number of registered manufacturers and also has discretion to give each of the factors listed in 21 U.S.C. § 823(a) the weight she deems appropriate; (3) Respondent has not established that there is a need for a second cultivator of marijuana; (4) there is no competition issue in this case because Respondent is seeking a contingent registration while he seeks a pharmaceutical company that would develop a medicinal marijuana plant product, which would violate the DEA's policy against shelf registration; (5) Respondent has not shown that his registration would result in a pharmaceutical company developing a marijuana plant drug product; (6) competition in the manufacture of marijuana, as the term "competition" is used in 21 U.S.C. § 823(a)(1), is afforded by the bidding process to obtain contracts with NIDA to supply marijuana for research because (a) there is extremely limited demand for marijuana for research and it therefore makes no sense to treat it like a Schedule II commercial drug, (b) the bidding system is reasonable because marijuana is the most commonly abused drug, and (c) the competitive bid system is more consistent with the Single Convention than registering multiple marijuana producers; (7) there is no allegation or proof that Respondent has not complied with applicable state and local statutes and regulations, but Dr. Doblin admittedly abuses marijuana routinely and he has also diverted marijuana from a compassionate use patient to an analytical laboratory; (8) Respondent has not proposed any technical advances in cultivating marijuana or indicated any plans to develop new substances, nor has he explained how he

would control potencies or alter marijuana's constituents, in contrast to the various developments to which Dr. ElSohly testified; (9) Dr. Doblin has no conviction record; (10) the Government does not assert that Respondent will not maintain effective controls against diversion, but his application is nonetheless deficient because of his lack of experience with controlled substances; (11) Dr. Doblin's conduct is relevant inasmuch as he asked Respondent to file the instant application and assisted Respondent throughout this process and would designate the researchers who would receive marijuana from Respondent if he obtains a registration; (12) Dr. Doblin believes that marijuana should be legalized, abuses marijuana routinely, and diverted marijuana intended for consumption by an experimental use patient to Chemic, which indicates that he would not be adverse to acting outside the scope of the DEA's regulations; (13) Respondent, by seeking to supply marijuana to researchers who have not undergone the Public Health Service review process, is inviting the DEA to violate Health and Human Services policy, which the DEA may not do; and (14) there is no reason to register Respondent in order to have marijuana available in the event of an emergency at the National Center.[135]

Respondent contends, in substance, that as a threshold matter, pursuant to 21 U.S.C. § 823, if an application does not pose an increased risk of diversion and the applicant meets the other requirements, the DEA must grant the application regardless of whether there is an existing adequate supply. Respondent further contends that registering Respondent as a bulk manufacturer of marijuana would be consistent with the public interest because: (1) creating an alternative to the current NIDA-controlled monopoly would promote the advancement of science and research by adding competition without increasing the risk of diversion, citing *Noramco of Delaware v. DEA*, 375 F.3d 1148, 1153 (D.C. Cir. 2004), for the proposition that DEA may limit competition only in order

[135] The Government offered into evidence at the hearing various final orders issued by the DEA's Deputy Administrator. I rejected these proffered exhibits because they were not based upon an adjudicatory proceeding, but rather on the investigative file after the respondents waived their rights to a hearing. The Government contends that this ruling was in error and requests that I admit the exhibits at issue, on grounds that they are admissible hearsay and provide general information about marijuana. I adhere to my ruling, as these final orders are based on reports of investigations rather than evidence adduced in adjudicated proceedings. With respect to the contention that these final orders provide general information about marijuana, there is sufficient information in the record

to control diversion; (2) the current system does not provide an adequate and uninterrupted supply of marijuana for legitimate purposes, emphasizing that NIDA does not make marijuana available for all legitimate medical and scientific research, but only to those studies it considers the most likely to produce usable and essential data, that NIDA has determined that the goal of any research for which it will supply marijuana must be to determine whether cannabinoids administered through a delivery system other than smoking can meet the FDA's standards for medical products, and that NIDA does not meet the legitimate needs of a sponsor seeking to develop marijuana into an FDA-approved pharmaceutical product; (3) Respondent has agreed to provide a defined marijuana product that will suit both MAPS' and researchers' needs, and Respondent expects to be able to provide a more uniform product than the National Center currently does; (4) FDA, not the DEA or NIDA, has the responsibility for determining whether marijuana has a medical use, and DEA cannot use its registration authority to prevent a sponsor from seeking FDA approval of marijuana, especially inasmuch as the parties stipulated that "research continues about how cannabis may be of therapeutic benefit to patients;"[136] (5) NIDA's monopoly on the supply of marijuana to researchers fails to fulfill the requirement of 21 U.S.C. § 823(a)(1) that marijuana be supplied under adequately competitive conditions, and opening the contract to supply marijuana to NIDA to competitive bidding does not cure the defect, noting particularly that (a) the contract requires other services, such as analysis of samples, as well as the manufacture of marijuana, (b) the contract assures only that NIDA pays a competitive price, but not that the price researchers pay is competitive, (c) although NIDA supplies marijuana at cost, there are additional benefits to competition, including improved product quality and reliability, among others,[137] and (d) for those researchers whom NIDA refuses to supply, competition as to cost is irrelevant inasmuch as they have no other supplier; (6) even if the current system of supplying marijuana produced an adequate and uninterrupted supply under adequately competitive conditions, there is no evidence that registering Respondent would increase the risk of diversion, inasmuch as (a) Respondent's security

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on the subject.

[136] Prehearing Ruling issued May 23, 2005; ALJ exhibit 5, p. 1.

[137] Respondent quotes *Noramco*, 375 F.3d at 1158.

measures satisfied DEA requirements, (b) the Deputy Administrator found in *Chattem Chemicals, Inc.*, 71 Fed. Reg. 9834 (Feb. 27, 2006) that inasmuch as DEA establishes manufacturing and procurement quotas to avoid overproduction and the demand for retail controlled substances was the major factor in increased bulk manufacturing, registering an additional importer would not likely be a significant cause of diversion at the retail level, and (c) in June 2005 the DEA agreed to seek United Nations approval to increase the National Center's manufacturing quota from 913 to 4,500 kilograms, which it would not have done if it thought that increase would lead to increased diversion; (7) information about marijuana as a drug of abuse in general does not establish that registering Respondent would increase the risk of diversion; (8) there is no evidence that MAPS' role as a sponsor of developing marijuana as a pharmaceutical product would increase the difficulty of preventing diversion, emphasizing that MAPS has sponsored DEA-licensed researchers in various Phase I and II drug trials of controlled substances with no allegation of diversion, that neither Dr. Doblin nor any other MAPS personnel or any other unauthorized person would have access to the marijuana Respondent would grow, and that Dr. Doblin's personal use of marijuana is irrelevant and evidence on that issue should not have been admitted; (9) Respondent has demonstrated that he has and will continue to comply with applicable state and local law; (10) registering Respondent would promote scientific and technical advances because (a) Respondent intends to grow marijuana indoors, which would provide more control over environmental factors (b) Respondent seeks to grow marijuana in order to research development of a vaporizer as an alternative to smoked marijuana, (c) an alternative source to the National Center's marijuana would provide an opportunity to validate and replicate Dr. ElSohly's discoveries and techniques, and (d) registering Respondent would enable research into possible clinical uses of marijuana for which NIDA has refused to provide material; (11) Respondent's lack of patents should not weigh against his application inasmuch as the University of Mississippi has been the only registered cultivator of marijuana for thirty years; (12) Respondent has no prior conviction relating to controlled substances; (13) although Respondent does not have past experience in manufacturing controlled substances, Dr. ElSohly is the only person in the country with relevant experience in the legal manufacture of marijuana, and the FDA has only recently issued guidelines for

developing medicinal botanical products: there are thus few if any applicants with the expertise in botanicals who would also have experience in chemical manufacture, and Respondent has significant experience in cultivating and propagating plants; and (14) all other considerations relevant to the public health and safety weigh in favor of granting Respondent's application, asserting that this factor cannot be used to reconsider evidence related to another of the § 823(a) factors, and further contending that (a) the support of various members of Congress for Respondent's application weighs in favor of granting it, (b) Dr. Robert's testimony establishes that there is real political opposition in the government to the development of botanical marijuana and that this opposition constricts medical research by restricting the amount of marijuana available for it, and (c) Respondent's application is not premature and seeking the registration before lining up researchers is prudent, especially in light of the length of time that has elapsed since Respondent filed the instant application.

Respondent further asserts that granting him a registration would be consistent with all laws, treaties and conventions. With respect to the Single Convention, Respondent asserts that the Single Convention repeatedly refers to "cultivators" as plural, and nowhere suggests that the number of cultivators be limited to one; although it is unclear whether the United States agency contemplated by the Single Convention is NIDA or the DEA, it is clear that there is an agency that fills that role; if it is acceptable for Dr. ElSohly to not deliver his non-NIDA marijuana to a government agency it is acceptable for Respondent to act likewise, inasmuch as he would be processing the plant into a form acceptable for medical use; and England, a signatory to the Single Convention, has created a system of constructive possession for all licensed manufacturers, and the Government does not contend that this system violates the Single Convention.

DISCUSSION

As noted above, the Deputy Administrator is to register an applicant to manufacture a Schedule I controlled substance if she determines that such registration is consistent with the public interest and with the United States' obligations under international treaties.

I. The Single Convention

As discussed above, the Single Convention specifies that signatory parties have certain responsibilities with respect to marijuana and that such parties are to establish a single government agency to discharge those responsibilities. As Respondent asserts in his brief, it is not clear whether the DEA or NIDA is that agency.[138] The DEA, through its registration process, performs the licensing function, and, through its quota-setting process, determines the total amount of marijuana the National Center is permitted to produce, but NIDA determines how much marijuana the National Center produces for it. It is noteworthy that no government agency takes physical possession of the National Center's crop; it appears, however, from the United Kingdom's regulatory scheme described above that the parties to the Single Convention are free to construe the term "physical possession" as they see fit.

It also appears, although it is not entirely clear, that the marijuana grown by the National Center or by any other registrant for utilization in research would qualify as either "medicinal" within the meaning of Article 1, Paragraph (1)(o),[139] or as "special stocks" within the meaning of Article 1, Paragraph (1)(x),[140] and that therefore the government monopoly on importing, exporting, wholesale trading, and maintaining stocks would not apply. I therefore find that the Single Convention does not preclude registering Respondent.

II. The Statutory Factors

A. Section 823(a)(1)

21 U.S.C. § 823(a)(1) requires consideration of maintaining effective controls against diversion by limiting the manufacturing of Schedule I or II controlled substances "to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research and industrial purposes." Respondent emphasizes that in *Noramco of Delaware v. DEA*, 375 F.3d 1148 (D.C. Cir. 2004), the United States Court of Appeals for the District of Columbia Circuit found that "The stated purpose of section 823(a)(1) is

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[138] Respondent's Proposed Findings of Fact, Conclusions of Law and Argument, p. 66.
[139] Single Convention, art. 1, para. 1(o).
[140] Single Convention, art. 1, para. 1(x).

to effectively control against diversion and it expressly directs the DEA to limit competition only as a means to achieve 'maintenance' of such control."[141] I note, however, that in the same opinion the court apparently found that it was not improper for the Deputy Administrator to consider the adequacy of competition;[142] I therefore address both issues.

1. Controls Against Diversion

Respondent testified that he would grow marijuana in a climate-controlled room that had one wall in the earth and had only one door, that the drying area would be connected to the cultivation room, and that the DEA personnel who visited the University of Massachusetts to inspect the proposed cultivation and drying area said that they thought the area could be made secure. There is no evidence or contention that either Respondent or anyone working with him would be likely to divert the marijuana from the growing or drying or storage areas. I also note that in his August 2002 answers to the DEA's questions, Respondent stated that he intended to grow about twenty-five pounds (dry weight) of marijuana in the first year of cultivation if his application is granted, and there is no evidence – nor does the Government contend – that his intentions are otherwise. I therefore find that it is unlikely that the marijuana that Respondent would grow would be diverted from the University of Massachusetts' facility.

There remains the question of whether marijuana would be diverted after it left the University of Massachusetts. In this respect, the Government emphasizes that Dr. Doblin believes that marijuana should be available as medicine and for non-medical purposes as well, and that the incident in which Dr. Doblin arranged for marijuana from a user in the compassionate use program to be sent to the Drug Detection Laboratory and then to Chemic demonstrates that he would not be averse to operating outside of the DEA's regulatory framework.

The record in this proceeding demonstrates that Dr. Doblin disagrees with the DEA's position on the dangers of marijuana use, and it also demonstrates, as the Government asserts, that Dr. Doblin and MAPS are the sponsors of Respondent's application and would determine the recipients of the marijuana that Respondent would

[141] *Noramco*, 375 F.3d at 1153.
[142] *Id.* at 1154, 1157.

grow if he becomes registered to do so. However, the record also establishes that MAPS and Dr. Doblin would not at any time have physical possession of that marijuana and, perhaps most importantly, that Respondent would send marijuana only to researchers who hold DEA registrations and, therefore, have the requisite approval from the Department of Health and Human Services, including findings that the researcher is qualified and competent, that the research protocol is meritorious, and that the research project has procedures in place to adequately protect against diversion of the marijuana. In these circumstances, I conclude that there is minimal risk that the marijuana that Respondent would cultivate would be diverted.

2. Competition

a. Adequacy of Supply

Although the record contains evidence that there have been some problems with the marijuana that the National Center produces, I find that a preponderance of the record establishes that the quality is generally adequate. I further find that there is no evidence that researchers whom NIDA approves to obtain marijuana have experienced difficulties in obtaining marijuana from the National Center when they need it.

The record does establish, however, that NIDA's system for evaluating requests for marijuana for research has resulted in some researchers who hold DEA registrations and requisite approval from the Department of Health and Human Services being unable to conduct their research because NIDA has refused to provide them with marijuana. I therefore find that the existing supply of marijuana is not adequate.

b. The Policy Against "Shelf Registrations"

As discussed above, the Government contends that registering Respondent would violate the DEA's policy against contingent registrations because Respondent has not shown that his registration would result in a pharmaceutical company developing a drug product from plant marijuana.

I disagree. Respondent is not obligated to show that his registration will lead to a pharmaceutical product but, rather, that he will use his registration to produce marijuana that will be used in legitimate research. That, Respondent has done.

c. Competition via the Process for Awarding NIDA's Contract

The Government also asserts that the process by which NIDA awards the contract to grow marijuana for research provides adequate competition inasmuch as the demand for licit marijuana is extremely limited and marijuana is the most commonly abused drug in the United States. The question is not, however, whether the NIDA process addresses that agency's needs, but whether marijuana is made available to all researchers who have a legitimate need for it in their research. As discussed above, I answer that question in the negative.

It is also undisputed that the NIDA contract requires the contractor to analyze samples of marijuana supplied by law enforcement agencies, a separate activity from cultivating marijuana for research purposes and a requirement that a qualified cultivator may not be able to fulfill.

I find that the NIDA contractual process does not, in the context of this case, render competition in the manufacture of marijuana adequate.

3. Conclusions with respect to Section 823(a)(1)

I find that if Respondent's application is granted, the risk that the marijuana that he would cultivate would be diverted is minimal and that competition in the manufacture of marijuana for research purposes is inadequate. I therefore find that this factor weighs in favor of granting Respondent's application.

B. Section 823(a)(2)

Section 823(a)(2) requires consideration of the applicant's compliance with applicable law. There is neither evidence nor contention that Respondent has not complied with applicable laws and I therefore find that this factor weighs in favor of granting Respondent's application.

C. Section 823(a)(3)

Section 823(a)(3) calls for consideration of the promotion of technical advances in the art of manufacturing controlled substances and in developing new substances. It is undisputed that Respondent has no experience in manufacturing or otherwise handling controlled substances. He does have considerable experience in cultivating medicinal plants, which might promote technical advances in the cultivation of marijuana or in

developing new medications from it. I find, however, that there is not sufficient evidence in the record on which to base a finding as to whether granting Respondent's registration would promote technical advances.

D. Section 823(a)(4)

Section 823(a)(4) requires consideration of the applicant's prior conviction record under laws relating to the manufacture, distribution, or dispensing of controlled substances. It is undisputed that Respondent has never been convicted of any violation of any law pertaining to controlled substances, and I therefore find that this factor weighs in favor of granting the application.

E. Section 823(a)(5)

Section 823(a)(5) requires consideration of the applicant's past experience in manufacturing controlled substances and the existence of effective controls against diversion. As discussed above, Respondent has no experience in manufacturing controlled substances, but does have experience in growing medicinal plants. As also discussed above, I find that the risk of diversion that would result from granting Respondent's application is minimal. I therefore find that this factor weighs in favor of granting the application.

F. Section 823(a)(6)

Section 823(a)(6) requires consideration of other factors relevant to public health and safety. I have discussed Dr. Doblin's use of marijuana and his attitude toward the regulation of marijuana above, and need not repeat that discussion here.

The Government contends that granting Respondent's application would amount to circumventing the Department of Health and Human Services' policy with respect to providing marijuana to researchers, and that the DEA has no legal authority to do so. But as quoted above, the NIH Guidance by its own terms applies to marijuana that the Department of Health and Human Services makes available, not marijuana that might be available from some other legitimate source. I therefore find that the NIH Guidance is not a factor in determining whether Respondent's application should be granted.

CONCLUSIONS

I conclude that granting Respondent's application would not be inconsistent with the Single Convention, that there would be minimal risk of diversion of marijuana resulting from Respondent's registration, that there is currently an inadequate supply of marijuana available for research purposes, that competition in the provision of marijuana for such purposes is inadequate, and that Respondent has complied with applicable laws and has never been convicted of any violation of any law pertaining to controlled substances. I therefore find that Respondent's registration to cultivate marijuana would be in the public interest.

RECOMMENDED DECISION

I recommend that Respondent's application be granted.

Dated: February 12, 2007

Mary Ellen Bittner

Mary Ellen Bittner
Administrative Law Judge

JLS

CERTIFICATE OF SERVICE

This is to hand certify that the undersigned on February 12, 2007, caused a copy of the foregoing to be delivered ~~via interoffice mail~~ to counsel for the Government, Brian Bayly, Esq., Office of Chief Counsel, Drug Enforcement Administration, Washington, D.C. 20537, and a copy to be ~~mailed, postage paid~~, to counsel for Respondent, Julie M. Carpenter, Esq., Jenner & Block, 601 Thirteenth Street, N.W., Suite 1200 South, Washington, D.C. 20005.

hand delivered JLS

Janice Lee Stuell for

Patricia A. Medico
Secretary to Mary Ellen Bittner
Administrative Law Judge