UNITED STATES DEPARTMENT OF JUSTICE
DRUG ENFORCEMENT ADMINISTRATION

IN THE MATTER OF	)	Docket No. 05-16
LYLE E. CRAKER, PH.D.	)	

GOVERNMENT'S PROPOSED FINDINGS OF FACT, CONCLUSIONS OF LAW AND ARGUMENT

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Pursuant to 21 C.F.R. § 1316.64, the United States Department of Justice, Drug Enforcement Administration (DEA), by and through the undersigned attorney, respectfully submits the following proposed findings of fact, conclusions of law and argument.

I. PROPOSED FINDINGS OF FACT

A. Procedural Facts

1. On June 28, 2001, Lyle E. Craker, Ph. D. (Dr. Craker), University of Massachusetts, Department of Plant and Soil Science, filed a new application with DEA to manufacture (cultivate) marijuana, a Schedule I controlled substances. (ALJ-1; G-1)[1]
2. On December 10, 2004, DEA issued an order to show cause (OTSC). (ALJ-1) The OTSC sought to deny Dr. Craker's application to manufacture marijuana "for reason that DEA cannot determine that such registration would 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 (Single Convention), March 30, 1961, 18 U.S.T. 1407, ..." (ALJ-1)
3. On January 5, 2005, Dr. Craker timely requested a hearing to contest the OTSC. (ALJ-2) Subsequently, two attorneys entered appearances to

1 "ALJ- " refers to an Administrative Law Judge Exhibit. "G- " refers to a Government Exhibit. "R- " refers to a Respondent (Dr. Craker) exhibit. "Tr.- , l. " refers to page(s) and line(s) in the hearing transcript. "FOF- " refers to the numbered paragraphs found under the "Operative Facts" section of this brief.

represent Dr. Craker. (ALJ-3, 4) (Hereinafter, the applicant will be referred to as either "Dr. Craker" or "Respondent.")

4. On May 23, 2005, the Administrative Law Judge (ALJ) issued her Prehearing Ruling. The Prehearing Ruling defined the umbrella issue as follows: "Whether a preponderance of the evidence establishes that granting Respondent's application for registration as a manufacturer of the Schedule I controlled substances would be in the public interest as that term is used in 21 USC § 823(a)." (ALJ-5, pg 1)

5. The Prehearing Ruling set forth the parties' stipulations, which will be set forth under the "Operative Facts" section, *infra*. The Prehearing Ruling also set the dates of the hearing for August 22 through August 26, 2005, September 26 through September 30, 2005, and December 12 through December 16, 2005. (ALJ-5, pg. 3; ALJ-8) (The hearing for September 26 through September 30 was cancelled, but the hearing resumed on December 12, 2005, and concluded on December 16, 2005.)

6. On August 12, 2005, the ALJ issued a "Memorandum to Counsel and Ruling on Motion in Limine." This ALJ ruling was in response to the Government's motion to exclude certain testimony and exhibits that Respondent tendered to introduce at the hearing. (ALJ-9) The ruling noted that the Government argued that certain exhibits were irrelevant because they concerned the relative benefits and risks of using marijuana as medicine and such issues were not addressed under the factors listed in 21 U.S.C. § 823(a). The ruling also noted that the

Government sought to exclude anecdotal testimony and documents about the alleged medical benefits of marijuana. The Government also argued that for similar reasons the testimony of Respondent's pharmaceutical expert, Irwin Martin, Ph.D., (Dr. Martin) should be excluded.

7. The ruling noted that Respondent filed a response in opposition to the Governments' motion in limine. (ALJ-9, pg. 2) The ruling noted that Respondent argued that DEA should err on the side of admissibility and that the contested evidence was admissible under 21 USC § 823(a)(6).

8. The ALJ ruled "... evidence pertaining to marijuana's therapeutic uses is irrelevant to the issue of whether Respondent's registration would be consistent with the public interest." (ALJ-9, pg. 4) The ruling granted the Government's motion in limine except to the extent that Respondent's evidence related to evidence about the difficulty of obtaining marijuana for research from the National Institute of Drug Abuse (NIDA). *Id.* The ruling also did not exclude the testimony of Respondent's pharmaceutical expert, Dr. Martin. *Id.*

B. Issue

"Whether a preponderance of the evidence establishes that granting Respondent's application for registration as a manufacturer of the Schedule I controlled substances would be in the public interest as that term is used in 21 USC § 823(a)." (ALJ-5, pg 1)

C. Operative Facts

Stipulations

1. Marijuana is a Schedule I hallucinogenic controlled substance under 21 CFR § 1308.11(d)(20) and 21 USC § 812(10) (2004).
2. Dronabinol (synthetic), in a sesame oil and encapsulated in a soft gelatin capsule in a United States Food and Drug Administration (FDA) approved product, is a Schedule III hallucinogenic controlled substance. 21 CFR § 1308.13(g)(1). Marinol is a brand of dronabinol. *Physician's Desk Reference*, 56th Edition, Medical Economics Company, Montvale, New Jersey (2002), pg. 3325.
3. Research continues about how cannabis may be of therapeutic benefit to patients.
4. Because THC (one of the components of cannabis) offers therapeutic benefits to some patients, the FDA has approved a synthetic version of THC, called dronabinol, in the form of a pill for use as a therapeutic drug.
5. As of May 18, 2005, there is in effect a federal injunction prohibiting the United States from prosecuting some patients in California who grow and use marijuana for medicinal purposes. (Subsequent to the parties' stipulations but prior to the commencement of the hearing on December 12, 2005, the Supreme Court, on June 6, 2005, overturned the Federal injunction in *Gonzales v. Raich*, 125 S. Ct. 2,195 (2005). The Government would request the ALJ and the Deputy Administrator to take official notice of the *Gonzales v. Raich* Supreme Court decision pursuant to 5 USC § 556(e) of the Administrative Procedure Act.)
6. The federal government has established and maintains a compassionate

use program under which it provides marijuana cigarettes to some patients for their medical use.

7. England is a signatory to the United Nations Single Convention on Narcotic Drugs. (The record correctly reflects that the United States is also a signatory to the United Nations Single Convention on Narcotic Drugs. (R-2, pg. 3))

8. GW Pharmaceuticals has developed a cannabis-based oral spray, trademarked and patented as Sativex®, as a means of delivering the therapeutic benefits of cannabis to patients. As of April 2005, that product has been approved for marketing in Canada. (Both parties put into evidence additional testimony and documents concerning GW Pharmaceuticals and Sativex®, *infra*.)

Operative facts from the evidentiary hearing

(a) Testimony of Irwin G. Martin, Ph. D.

9. Irwin G. Martin, Ph. D., (Dr. Martin) is a former executive in the pharmaceutical industry. (Tr.-83, l. 4-22, 1-2; R-11) He worked at various pharmaceutical companies and represented such companies in working with FDA to obtain approval to market new drug products. (Tr.-86-87, l. 20-22, 1-20; Tr.-87-88, l. 21-22, 1-17)

10. Dr. Martin was qualified by the ALJ as an expert in new drug development. (Tr.-83, l.16-21)

11. Dr. Martin testified that initially the Research Division (of the pharmaceutical company) would discover a compound that had medicinal potential and would do initial testing on animals. (Tr.- 90, l. 5-18)

12. Then the management team decides whether human testing would be viable and, if so, puts forth an Investigational New Drug Application (IND). (Tr.-90-91, l. 19-22, 1-6)

13. Next, the FDA has thirty days to review the IND, and if the FDA within that time period ahs no objections to the IND, the IND goes into effect. (Tr.-92, l. 1-12)
14. The next step for the pharmaceutical company is to test the drug on healthy volunteers in Phase I to determine the safety of the drug and how the body handles the drug. (Tr.-92-93, l. 13-22, 1-4)
15. In Phase II, the number of patients using the experimental drug increases to obtain more certainty as to whether the drug has efficacy. (Tr.-98, l. 1-16)
16. In Phase III, large numbers of patients are recruited to further study safety and efficacy. (Tr.-98-99, l. 19-22, 1-6) When Phase III is completed, the pharmaceutical company then presents the studies to FDA to have FDA determine if the drug is suitable for marketing. (Tr.-99, l. 7-10)
17. The research step (before the IND process commences) could take up to ten years, and the IND process itself may take seven to eight years before it is brought to market. (Tr.-104-105, l. 14-22, 1-2)
18. Dr. Martin explained that FDA's primary responsibility is to assure public safety and not to assure that new drugs are developed. (Tr.-108, l. 1-7) The main criteria for FDA, as the drug moves to the marketing stage through a New Drug Application (NDA), are safety, efficacy and quality. (Tr.-108, l. 10-21)
19. Dr. Martin testified that it is necessary to test for consistency from batch to batch of the new drug product to ensure that what is tested in Phase I is the same as is tested in Phase 2; the process is conducted by a number of techniques, which are very complex analytical tools in a fairly rigorous process. (Tr.-109-110, l. 13-22, 1-5)
20. Single-small molecule products are much easier to maintain consistency

than are complex products such as botanicals. (Tr.-110-111, l. 6-22, 1) Dr. Martin was aware that FDA released guidelines on how to submit an NDA for botanicals, and it was Dr. Martin's opinion that FDA was willing to accept a botanically derived product and hold it to the same standards as other products. (Tr.-111-112, l. 12-22, 1) Dr. Martin admitted, however, that he was no longer active in the industry and that the FDA botanical guidelines were released just last year. *Id.*

21. Dr. Martin explained that if a drug company cannot maintain a consistent product, then a drug cannot be developed. (Tr.-120, l. 11-20) If there is a pharmaceutical change in the product that is out of the company's control or if the company seeks to make a better drug product, the company must determine whether the new product is equivalent of the original product; if that is not possible the company must start all over again. (Tr.-120-122, l. 21-22, 1-11)
22. On cross-examination, Dr. Martin testified that he never developed a drug that had abuse potential and never dealt with developing a drug that would be controlled. (Tr.- 125-126, l. 15-22, 1-8)
23. Dr. Martin estimated that for every ten INDs submitted only one would move to an NDA to be marketed. (Tr.-127, l. 10-20)
24. Dr. Martin noted that another hurdle to developing a new drug [other than consistency of supply] was the cost of the development, which he estimated at $800,000,000; this estimate included opportunity cost, i.e. not just the out-of-pocket expenses. (Tr.-133-134, l. 7-22, 1-22)
25. Dr. Martin agreed that drug companies encountered more hurdles with developing drugs because of the restrictions on controlled substances, the disinclination of physicians to prescribe controlled substances as opposed to other drugs, and the extra delays in reaching the market. (Tr.-140, l. 1-3; Tr.-142-143, l. 16-22, 1; R-1, pg. 219) Dr. Martin

testified on cross-examination that the fact that a drug company would have to petition [DEA] to place a Schedule I product in a lower schedule would be another hurdle to drug development. (Tr.-159-160, l. 22, 1-12)

26. Another factor to consider before developing a new drug product is the existence of competing drug products. (Tr.-143, l. 3-9)

27. Dr. Martin testified that his expertise was not in marketing but that he was "...on the listening end." (Tr.-148, l. 2-14) Dr. Martin also divulged that he had no personal experience in botanical development. (Tr.-156, l. 2-14)

28. Dr. Martin indicated there were other factors that were hurdles to developing a new drug, i.e. interaction with other drugs (typically discovered before an IND is submitted (Tr.-149-150, l. 19-22, 1-10), side effects (which may be the result of an inability to make the drug product consistently (Tr.-150, l. 11-17)), and patent issues including the possibility of obtaining patents for the drug deliver system. (Tr.-150-151, l. 18-22, 1-12)

(b) **Testimony of David Auslander, Ph. D.**

29. David Auslander, Ph. D., (Dr. Auslander) as an expert pharmaceutical consultant, is President of DEATech Associates, which provides expert advice on various issues dealing with drug development. (Tr.-1975-1976, l. 1-22, 1-22; Tr.-1977, l. 1-3; R-83)

30. Dr. Auslander was responsible for pharmaceutical process validation. (Tr.-1978-1979, l. 14-22, 1-22) Included in Dr. Auslander's relevant experience were his work in pharmaceutical development and particularly his work with FDA for pharmaceutical drug development specifications. (Tr.-1977-1978, l. 4-22, 1-13; Tr.-1980, l. 9-17)

31. Dr. Auslander's experience also included conducting studies to provide data that would generate information regarding drug products' purity

and quality aspects to ensure that formulations were adequate. (Tr.-1981-1982, l. 12-22, 1) His experience also included developing the manufacturing process for various phases of clinical development and developing the technical data to support formulation and process development all under FDA requirements. (Tr.-1982, l. 1-12.)

32. Dr. Auslander's past experience entailed being responsible for validations and pre-approved inspections to ensure that the commercial plant as designated in the NDA application is ready to produce the product under the specifications and quality standards as specified in the NDA. (Tr.-1985-1986, l. 13-22, 1-9) Dr. Auslander also was responsible for the validation for the drug substance and drug product to ensure consistent quality for the present and in the future. (Tr.-1986, l. 10-17) His experience includes auditing to ensure compliance with, *inter alia*, FDA requirements, and he was involved with validation programs, which are part of the FDA expectation program. (Tr.-1989-1990, l. 17-22, 1.-18-22, 1-19)
33. Dr. Auslander was very familiar with the three IND Phases and his work experience included working with INDs in all three Phases. (Tr.-1987-1988, l. 21-22, 1.-4)
34. Specifically, Dr. Auslander had experience with developing controlled substances as a marketable drug product under FDA approval. (Tr.-1988, l. 5-9)
35. Dr. Auslander also had experience with botanical products in the later stages in developing drug products. (Tr.-1990-1991, l. 20-22, 1-16)
36. Dr. Auslander was qualified by the ALJ as an expert in pharmaceutical drug development. (Tr.-1994, l. 4-11)
37. Dr. Auslander explained that a botanical drug product was one of plant or vegetable origin. (Tr.-1991-1992, l. 17-22, 1-4) FDA has published

standards for botanicals, which are very complex products. (*Id.*; G-92A)

38. Dr. Auslander explained the difference between botanical drug products and synthetic drug products; Synthetics have a very established purity and can be more readily quantified, qualified and understood over time while botanicals are much more complex because they have a variety of constituents that are not easily identified and require tremendously greater effort, time, resources and capabilities to establish. (Tr.-1994-1995, l. 14-22, 1-15). Dr. Auslander also explained "... that the pathway for a pure drug substance can use more defined classical techniques, as opposed to a botanical, which are a lot more unknown materials." (Tr.-1996, l. 2-5)

39. Dr. Auslander explained that there were additional hurdles in developing a botanical, as opposed to a synthetic, in going through the three IND phases; the drug developer must be able to isolate and distinguish the botanicals components, and such a process would require more resources. (Tr.-1998, l. 7-20) The problems are compounded if the botanical have components of varying pharmacological activities. (Tr.-1999-2000, l. 8-22, 1) If the benefit of the intended indication is very critical, then FDA might be more lenient in approval. (Tr.-2000, l. 2-10; Tr.-2008-2009, 21-22, 1-10) (Dr. Auslander defined "early stage" as the IND stage. (Tr.-2009-2010, l. 11-22, 1-3)) But when the drug developer reaches Phase III, FDA will expect a complete evaluation of what's involved in the botanical product; at this phase, FDA would like to see the chemical constituents characterized and quantified or at the least FDA would expect the "markers" to be well established. (Tr.-2000, l. 11-20; Tr.-2030-2031, l. 17-22, 1) [See FOF-44 for an explanation of what a "marker" is.]

40. Dr. Auslander further explained that it would be much more difficult to

develop a botanical drug than a synthetic in terms of maintaining the purity or consistency of the botanical. (Tr.-2000, l. 21 to Tr.-2002, l. 1) The same complexity problems for botanicals exist for safety and efficacy. (Tr.-2003, l. 10-20)

41. Some of the problems with botanicals can be avoided by extracting the active ingredient desired if the extracting procedure is standardized. (Tr.-2003-2004, l. 21-22, 1-15) But extractions can range from easy to exceedingly difficult. (T.-2004-2005, l. 16-22, 1-5)

42. The more constituents a botanical has, the more difficult it is to evaluate the botanical; with a 100 or more constituents, more interactions take, the chemistry is more complex, and the engineering that is required to isolate, quantify, establish and understand the botanical. (Tr.-2005-2006, l. 6-22, 1-5) A large number of constituents presents exponential, as opposed to linear, permutations. *Id.*

43. Dr. Auslander explained that under the FDA's Botanical Guidelines, FDA would allow a botanical drug developer to chemical identification by spectroscopic or chromatographic "fingerprints" for the various constituents contained in a botanical; a variety of tests are performed to give a truer understanding of what the botanical material looks like and how it should behave. (Tr.-2101-2011, l. 16-22, 1-21; G-92A, pg. 22) Under the botanical guidelines, FDA will accept alternative tests if spectroscopic or chromatographic procedures have not been developed for a botanical. (Tr.-2013-2014, l. 19-22, 1-11)

44. One of the methods to identify a botanical's constituents is to use a "marker," which is a consistent chromotagraphic response and a surrogate for an active constituent. (Tr.-2017-2018, l. 5-22, 1-11) If the markers were not consistent, there would be a problem that would necessitate working it out with the FDA.; such a problem would be a

hurdle to overcome before FDA would approve the botanical for marketing. (Tr.-2019, l. 4-21)

45. Dr. Auslander explained that one could use a biological assay of a botanical constituent by testing on animals to determine physiological responses but such tests still must be quantifiable and consistent. (Tr.-2014-2015, l. 12-22, 1-4)

46. Dr. Auslander, based upon the FDA botanical guidelines, noted that it was even more important to do biological or chemical assays on the botanicals constituents if the botanical drug substance is considered potent, toxic or addictive. (Tr.-2015-2016, l. 5-22, 1-17; G-92A, pg. 22)

47. Developing information about drug products and substances is placed into a Drug Master File (DMF) or in the NDA. (Tr.-2023, l. 6-19) There is a certain amount of allowance of what may be placed in a DMF, but if a DMF exists, one would expect information about botanicals constituents to be in the DMF. (Tr.-2023-2024, l. 20-22, 1-6)

48. FDA does not necessarily require a DMF to do Phase I or Phase II study in all cases if the DMF usually comes from a producer that is different from the sponsor itself. (Tr.-2024, l. 7-16) If the sponsor is developing the drug substances and the botanical itself, it may not necessarily have a DFM at the moment to target a Phase I and Phase II program. (Tr.2024, l. 16-20) Under these circumstances, a sponsor would provide an IND, which would contain the information; although such information needs to be documented, it would not have to be documented in a DMF. (Tr.- 2024-2025, l. 20-22, 1-3)

49. A DMF on file with the FDA may or may not note all the constituent "markers" of the botanical; DMFs vary although ideally the DFMs should contain all the information about the botanicals constituents. (Tr.-2029-2030, l. 22, 1-16)

50. If a drug company working on an IND obtains a botanical from facilities outside of their control, the company would need to ensure that the markers or surrogates for the botanical active ingredients are well established. (Tr.-2032, l. 1-16)

(c) **The FDA Process**

51. Based upon an affidavit from Douglas C. Throckmorton, M.D., Acting Deputy Director, Center for Drug Evaluation and Research, Food and Drug Administration, United States Department of Health and Human Services (HHS), the following information was entered into evidence about the FDA process relating to what a drug manufacturer must do in order to have a new drug approved for marketing to consumers (patients) in the United States. (G-92)

52. The Federal Food, Drug, and Cosmetic Act (FDCA), 21 USC § 321(g), defines the term "drug" in the 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), (B), or (C) … ." (G-92,¶ 3)

53. The FDCA, 21 USC § 321(p) defines the term "new drug" in the relevant part 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. (G-92, ¶ 4)

54. In order to be generally recognized as safe and effective (GRAS/E) within the meaning of 21 U.S.C. § 321(p), a drug must satisfy three criteria. First, the drug's reputation must be based on adequate and well-controlled studies that establish that the drug is safe and effective. Second, those studies must have been published in the scientific literature so that they are available to qualified experts. Third, qualified experts must generally recognize, based on those published studies, that the drug is safe and effective for its intended use. (G-92, ¶ 5)

55. Even if an active ingredient in drug product "A" has been previously approved as safe and effective in drug product "B", drug product "A" is considered a new drug if its particular formulation of active and inactive ingredients has not been previously approved or has not been found to be GRAS/E. (G-92, ¶ 6)

56. Any new drug product derived in whole or in part from marijuana is a new drug within the meaning of 21 USC § 321(p). Further, I am not aware of any evidence that any new drug product derived in whole or in part from marijuana is exempt from the new drug requirement of the FDCA. (G-92, ¶ 7)

57. No new drug product may 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). 21 USC § 355. (G-92, ¶ 8)

58. 21 USC § 355(b)(1) states that an NDA is required to contain the following:(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. (G-92, ¶ 9)

59. To develop the necessary reports of investigations that show that a particular drug product is safe and effective for a specific indication, an NDA sponsor must complete certain clinical investigations of that drug product. A clinical investigation is any experiment in which the drug is administered or dispensed to, or used involving one or more human subjects. Clinical investigations of unapproved new drugs are required to be conducted under valid INDs. See 21 USC 355(i) and 21 CFR Part 312. (G-92, ¶ 11)

60. A sponsor who intends to conduct a clinical investigation is required to submit an IND. 21 CFR § 312.23 sets out the information required to be contained in an IND. This information includes the name of the drug and all active ingredients, the structural formula of the drug, the formulation of the dosage form to be used, the route of administration, a brief summary of previous human experience with the drug, a brief description of the overall plan for investigating the drug product for the following year, and a protocol for the study. INDs are generally required to 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. (G-92, ¶ 12)

61. The clinical investigation of a previously untested drug product is generally divided into three phases. 21 CFR § 312.21. These phases are generally conducted sequentially, however they may overlap. The three phases of an investigation are as follows (G-92, ¶ 13):

62. (1) Phase 1: Phase 1 includes the initial introduction of an investigational new drug into humans. These studies are designed to determine the metabolism and pharmacologic actions of the drug product in humans, the side effects associated with increasing doses, and if possible, to gain early evidence of effectiveness. The total number of subjects generally ranges from 20 to 80. During this phase, information about the drug product's pharmacokinetics and pharmacological effects should be obtained to permit the design of a well-controlled, scientifically valid Phase 2 study. *Id.*

63. (2) Phase 2: Phase 2 includes the controlled clinical studies conducted to explore the effectiveness of the drug for a particular indication and to determine the common short-term side effects and risks of the drug product. Phase 2 studies usually involve no more than several hundred subjects. *Id.*

64. (3) Phase 3: Phase 3 studies are expanded controlled and uncontrolled clinical trials that are performed after preliminary evidence suggesting effectiveness of the drug product has been obtained, and are intended to gather the additional information about effectiveness and safety that is needed to evaluate the overall benefit-risk relationship of the drug and to

provide an adequate basis for labeling. Phase 3 studies generally include several hundred to several thousand subjects. *Id.*

65. The Act, 21 USC 355(d), provides the grounds under which FDA must refuse to approve an NDA. See also 21 CFR § 314.125. (G-92, ¶ 16)

66. Botanical products are finished, labeled products that contain vegetable matter as ingredients. Botanical products that meet the definition of a drug under 21 USC 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. (G-92, ¶ 17)

(d) **Testimony of Eric A. Voth, M.D.**

67. Eric A. Voth, M.D. (Dr. Voth) is a physician who is a member of the Fellow of American College of Physicians (FACP), which is an honorary bestowed upon those physicians for academic and professional accomplishments. (Tr.-1856, l. 1-2; Tr.-1857, l. 4-19) Dr. Voth's induction into the FACP was based mostly on his work in drug abuse. (Tr.-1857-1858, l. 20-22, 1-8)

68. Dr. Voth was a Board Certified physician by the American Board of Internal Medicine as of 1985, and his certification is current. (Tr.-1858-1859, l. 13-22, 1) About two-thirds to 70% of his medical practice is in internal medicine. (Tr.-1859, l. 10-18)

69. Dr. Voth is a clinical associate professor of internal medicine, University of Kansas School of Medicine, and he started this position in 1999. (Tr.-1863, l. 7-22; G-36, pg. 4)

70. Dr. Voth's medical practice also includes addiction treatment; Dr. Voth

was a medical director of a chemical dependency unit for ten years, and he continues to do consultations, referrals for treatment, detoxification and "a lot of drug policy work." (Tr.-1859-1860, l.19-22, 1-2)

71. In his medical practice, Dr. Voth has treated over 4,000 patients for addiction or abuse of controlled substances. (Tr.-1860, l. 3-14) This treatment includes those who have abused or become addicted to marijuana. (Tr.-1860, l. 15-19) Of such patients, about one-half abused other substances as well as marijuana, while a quarter of such patients were treated for marijuana abuse only. (Tr.-1860-1861, l. 20-22, 1-1-7)

72. One of the articles co-authored by Dr. Voth, *Medical Marijuana: A survey of Teenagers and their Parents*, Clinical Pediatrics, April/May 2001. (G-40) Survey samples were taken from adolescents and their parents in Virginia and Ohio; the samples adolescents generally did well in school, 10% smoked marijuana at least once and 6% smoked in the previous 30 days. (G-40, pg. 549, column 2) Lifetime use of marijuana was much lower than the national average for the adolescent age group. (R-40, pg. 549, column 3, last ¶) Lifetime us of marijuana was 27% of the parent respondents although none of the parents admitted current use. *Id.* The results of the surveys were that 28% of the parent group versus 55% of the teen group believed that passage of state referenda on medical marijuana would make it easier for teens to smoke marijuana for recreational purposes. (R-40, pg. 549, column 3, 1st incomplete ¶)

73. Dr. Voth also co-authored *The Use and toxicity of cannabis in teenagers*, In Recent Advances in Pediatrics, RSM Press, London, 2004. David, Timothy, ed. pg. 131-144. (R-36, pg. 8; R-41) Significant findings and conclusions were as follows. About 30% of American high school tenth-graders smoked cannabis in the last 12 months, and 20% of U.S. students of this age have smoked marijuana in the past 30 days

according to a 2002 NIDA study. (G-41, pg. 131, 143 and note 1) An estimated 10-20% of American and Australian adolescents who smoke cannabis become dependent on one or more drugs. (G-41, pg. 139, bottom of page) North American population surveys consistently suggest that 5-10% of those who have used cannabis more than once become dependent. (G-41, pg. 140, 1st full ¶)

74. Adverse effects from repeatedly smoking marijuana during adolescence include risk of motor vehicle and other accidents, respiratory disease, developmental delay, school underachievement and short-term memory defects. (G-41, pg. 132, 136, 1st, 2nd and 3rd full ¶¶) There are links between regular use of cannabis and later mental illnesses such as schizophrenia. (G-41, pg. 137, 1st full ¶) It is more difficult to learn and retain new material under the influence of cannabis. (G-41, pg. 137, 2nd full ¶)

75. Cannabis is usually abused by smoking in home-rolled cigarettes dainty pipes, hollowed-out stones or air-or water-cooled hookahs, known commonly as "bongs." (G-41, pg. 134) Smoking marijuana in a bong is a more efficient method of extracting THC because THC is more concentrated per inhalation. (G-41, pg. 135, 1st ¶)

76. Cannabis abuse and cannabis dependency are recognized disorders under the *Diagnostic and Statistical Manual* (DSM-IV) published and used as a diagnostic guide by the American Psychiatric Association. (G-41, pg. 140, Table 3, pg 141, 1st full ¶) In the late part of State 2 and Stage 3 of the DSM IV, an adolescent could suffer apathy and irresponsibility, academic under achievement, truancy, deterioration of ethical values such as lying and stealing, distortion of goals such as education and vocational goals, alienation and rebellion against family and society norms, promiscuity and running away from home. (G-41,

pg. 140, Table 3, pg. 141, 1st full ¶ and Table 4)

77. Dr. Voth first started to familiarize himself with marijuana research and policy issues in the mid-1970s. (Tr.-1861-1862, l. 12-22, 1) In 2000, Dr. Voth founded the Institute on Global Drug Policy, which is a drug policy think tank; Dr. Voth, as Chairman, put together position papers and policy statements. (Tr.-1862-1863, l. 19-22, 1-6) Dr. Voth is also a Consultant to the International Task Force on Strategic Drug Policy sponsored by the U.S. Department of the International Narcotics and Law Enforcement; this organization provides drug policy recommendations in various parts of the world and makes recommended changes. (Tr.-1871-1872, l. 19-22, 1-13; G-36, pg. 5)

78. Dr. Voth is on the Kansas State Board of Healing Arts, and in this capacity works with physicians who have drug or alcohol abuse or addiction problems. (Tr.-1864, l. 1-12) Dr. Voth is a member and former chairman for the Committee on Impairment and Advocacy, Kansas Medical Society; this committee is a liaison with impaired physicians to help them obtain treatment and return to practice. (Tr.-1866-1867, l. 10-22, 1-18; G-36, pg. 4) Dr. Voth also was the Chairman of the St. Francis Stormont-Vail Hospital, Physician Impairment and Advocacy Committee, from 1990-1994; this committee helped physicians with chemical dependency problems. (Tr.-1867-1868, l. 19-22, 1-20)

79. Dr. Voth was a member of the National Institute of Drug Abuse (NIDA), Epidemiology and Preventative Review in the late 1980s wherein Dr. Voth served on committees to oversee some grants that NIDA was considering relative to prevention and treatment programs. (Tr.-1864-1865, l. 13-22, 1-3) Dr. Voth is also a member, since 2003, of the National Advisory Committee for Centers of Substance Abuse

Treatment (CSAT). (Tr.-1865, l. 8-19). This committee reviews research and treatment grants and gives general advice to CSAT. (Tr. 1865-1866, l. 19-21, 1-9)

80. Dr. Voth also has reviewed books and participated in peer reviews of articles concerning, *inter alia*, marijuana abuse and addiction, marijuana's potential medical use, and marijuana's constituent. (Tr.-1868, l. 21 to 1871, l. 18; Tr.-1872, l. 14-20; G-36, pg. 7)

81. Based upon his education and experience, Dr. Voth studied and learned about marijuana and its constituents. (Tr.-1889-1890, l. 22, 3) Based upon his education and experience, Dr. Voth has learned about the physiological and psychological effects that marijuana and its constituents have on a human. (Tr.-1890, l. 4-8)

82. Dr. Voth has testified as an expert on marijuana in both Federal and State courts about three to five times. (Tr.-1890, l. 5-16)

83. Dr. Voth's extensive curriculum vita was admitted into evidence. (Tr.-1890-1891, l. 22, 1-3)

84. Dr. Voth was qualified by the ALJ as a medical expert in internal medicine and as an expert in marijuana as it pertains to its effects, abuse on humans and its constituents. (Tr.-1891, l. 4-10; Tr.-1892, l. 5-6; Tr.-1893, l. 1-13)

Dr. Voth's testimony on marijuana's constituents and their effects

85. Constituents are substances that constitute the drug, and in marijuana there area number of substances identified in the plant marijuana. (Tr.-1893, l. 15-21) About 480 substances have been identified in the marijuana plant and of these substances 66 have been identified as cannabinoids. (Tr.-1893-1894, l. 22, 1-4; Tr.-1904, l. 14-21) Cannabinoids are substances that resemble the major active ingredient Delta 9 THC or Delta 9 tetrahydrocannabinol. (Tr.-1894, l. 5-8)

Cannabinoids are segregated as a class of constituents because they are structurally very similar but not identical. (Tr.-12-22)

86. All 66 cannabinoids have not been studied so it is difficult to determine whether all are active. (Tr.-1895-1896, l. 18-22, 3; Tr.-1930, l. 3-9) There's a sense that some cannabinoids are more active than others; for example Delta 9 THC, Delta 8 THC and cannabidiol are cannabiniods that have been identified as being active. The drug Sativex uses Delta 9 THC and cannabidiol. (Tr.-1896, l. 3-8) But all the cannabinoids have relative degrees of activity. (Tr.-1896, l. 8-15)

87. The other 420 or so constituents contain tars and turpines and there is a concern of what happens when these substances enter a person's lungs; these constituents probably have a similar physiological effect to tobacco; these intoxicants likely do not have an intoxicating effect. (Tr.-1896-1897, l. 16-22, 1-18) Smoking marijuana can lead to problems with harshness on the throat and lungs. (Tr.-1909, l. 14-17)

88. Delta 9 THC acute effects include an intoxicated, "stoned," mood; there is also an effect on the coordination, driving skills concentration and short-term memory. (Tr.-1897-1898, l. 19-22, 1-22) Other effects include dysphoria, panic attacks, psychotic episodes or some sedation can occur. (Tr.-1898, l. 18-22) Dr. Voth defined "dysphoria" as an unexpected panic, an agitated kind of a feeling and potentially hallucinatory or transiently psychotic. (Tr.-1959, l. 13-19)

89. Long-term or chronic use can cause dependence or addiction, memory disorders, loss of concentration ability and an increase risk of psychotic or other psychiatric disorders; students' cognitive abilities and school performance are also effected. (Tr.-1899, l. 4-13)

90. One cannot suffer a fatal overdose of marijuana because, unlike sedatives, it does not suppress the activity in the brain, which leads to

the cessation of breathing. (Tr.-1899, l. 14-22)

91. The greater the amount of THC ingested, the greater the risk of dysphoria and panic attack; driving skills also are effected accordingly. (Tr.-1900, l. 1-12) Heart rate also increases at a more rapid rate when a greater amount of THC is ingested, but Dr. Voth was not aware of any studies that correlated the amount of increase in heart rate to the amount of THC ingested. *Id.*

92. When one smokes marijuana, there is a concern that there could be damage to the lungs and airways such as bronchitis; studies are conflicting whether smoking marijuana results in lung cancer or mouth cancer. (Tr.-1902, l. 5-17)

93. Relative to carcinogens, the literature has looked at this factor and not found a consistent pattern in the use of a higher THC concentration and inhaling less, necessarily, relative to intoxication. (Tr.-1902-1903, l.18-22, 1-2) A user may or may not smoke less marijuana because it has more THC; he may very well smoke more because he is "getting more stoned." (Tr.-1903, l. 7-15)

94. "Tolerance" occurs when a user is exposed to greater dosages without experiencing side effects; one can become tolerant to marijuana as one could become tolerant to liquor, i.e. one drinks significant amounts of alcohol can "hold his liquor." (Tr.-1903-1904, l. 16-22, 1-6) Tolerance occurs in marijuana based upon the effect of THC. (Tr.-1904, l. 7-9)

95. The common form of marijuana that is abused occurs in the plant form as opposed to its constituents; Dr. Voth was not aware of any abuse of Marinol or dronabinol. (Tr.-1904-1905, l. 22, 1-9; Tr.-1963, l. 11-16) Marijuana is one of the most commonly available and abused drugs in the United States. (Tr.-1941, l. 2-15; Tr.-1942, l. 1-19; G-45, pg. 2)

96. Although Dr. Voth indicated that he was not surprised that marijuana

dependency develops in only .5% of people who begin use after age 21, he noted that in earlier ages, such as age 14 or 15, the incidence of marijuana dependence is extremely high or 5 to 10% although estimates go as high as 30%.. (Tr.-1947, l. 7-22) Dr. Voth also explained that the earlier a person uses a drug, the more likely they are to become addicted to it; if one does not use any intoxicant until after age 21, his or her addiction chances diminish significantly. (Tr.-1947-1948, l. 22, 1-4) Dr. Voth also noted that the abuse problem would be significantly diminished if persons were never exposed to marijuana until after age 21, but that was not happening. (Tr.-1948, l. 2-6)

97. Dr. Voth is familiar with the product Sativex, which is manufactured by GW Pharmaceuticals; Sativex is formed by extracting Delta THC 9 and cannabidiol in roughly a one to one ratio. (Tr.-1905-1906, l. 10-22, 1-11)

98. While Sativex has a roughly a one to one ratio of Delta THC 9 to cannabidiol, the marijuana plant has a very high ratio of Delta 9 THC relative to cannabidiol. (Tr.-1906-1907, l. 19-22, 1-6)

99. When asked on cross-examination whether Sativex was equivalent to a herbal remedy, Dr. Voth replied "... Sativex is probably a generation beyond that. I do think, relative to marijuana, that that is sort of a throwback to the days of herbal remedies and witches' brews, yes." (Tr.-1934-1935, l. 20-22, 1-5)

100. Although the marijuana plant has all the 400 plus substances, there is a question as to how many of these substances are contained in Sativex; Sativex may contain some of these other constituents. (Tr.-1907, l.7-22) There are no clear definitions of what other constituents are contained in Sativex. (Tr.-1908, l. 2-6)

101. Dr. Voth is aware of Marinol and has used it in his practice; it's only

active constituent is Delta 9 THC. (Tr.-1908, l. 11-22) Marinol is primarily used as an appetite stimulant and to counteract nausea. (Tr.-1909, l. 1-7)

102. Although smoking marijuana can cause a harsh effect on the throat and lungs, these effects are not necessarily related to the amount of potency in the marijuana, but is due more to the fact that the marijuana is smoked. (Tr.-1909-1910, l. 18-22, 1)

103. Although Dr. Voth was aware of "street rumors" that the latter irritants were caused by seeds and stems, Dr. Voth had never seen anything systemic that indicated seed and stems cause any greater or lesser irritation. (Tr.-1910, l. 2-8)

104. Dr. Voth, during cross-examination, was asked (over objection) to comment on one of marijuana's short-term effects, which would be to relieve nausea. (Tr.-1957, l. 15-22) Dr. Voth responded that one of the best marijuana studies indicated that 25% of the patients in the study would not smoke marijuana because they did not like the effect and a "fairly significant percentage" did not obtain a beneficial effect. (Tr.-1958, l. 1-7) As Dr. Voth noted, any putative anti nausea effects can often be negated by dysphoria or euphoria effects for patients participating in smoked marijuana studies. (Tr.-1958-1959, l. 8-22, 1-4) Dr. Voth explained that a dysphoria effect was the opposite of a euphoric effect. Tr.-1959, l. 15-22)

105. Dr. Voth was also cross-examined on the effect of using a vaporizer to ingest marijuana. (Tr.-1964, l.17-20) Dr. Voth responded explained that vaporization changes the marijuana chemicals into a different phase, and Dr. Voth was unaware of any studies that indicate if the chemicals are filtered out or change into a liquid phase but are still ingested. (Tr.-1964-1965, l. 21-22, 1-9)

106. Dr. Voth was asked to comment on the following quote from the FDA botanical guidelines:

> "Furthermore, where the active constituents or other chemical markers are known and measurable, the amount in which they are present in the botanical drug substance should be declared. For a multi-herb substance, its composition should be expressed in terms of the relative ratio of the individually processed botanical drug substances or of the botanical raw materials before processing, whichever is appropriate." (G-92A, pg. 21, § 2, ¶ 2)

107. Dr. Voth explained that the latter paragraph indicated that it would be necessary to know what was in the botanicals and what the ratios are. (Tr.-1911, l. 1-22) Dr. Voth further explained that although the chemistry of marijuana is known, it would be extremely hard to reproduce 488 substances that have to be clearly reproduced and defined in a predictable manner to fulfill the FDA botanical guidelines criteria. (Tr.-1912-1913, l. 13-22, 1)

108. Based upon the FDA botanical guidelines that indicated a botanical would have to be identified by chemical spectroscopic or chromatographic fingerprint, Dr. Voth explained that the marijuana plant would have to undergo these identification processes to determine what the constituents are; these constituents would have to be characterized and defined. (Tr.-1913-1914, l. 2-20, 1-9; G-92A, pg. 22)

109. Based upon the FDA botanical guidelines, Dr. Voth noted that marijuana's 400 "plus" substances had to defined, marked and characterized. (Tr.-1914, l. 10-18; Tr.-1914-1915, l. 19-22, 1; G-92A, pg. 22)

110. Dr. Voth also noted that, based upon the FDA botanical guidelines' comments, a biological assay should be performed on marijuana (at least on the cannabinoids) because, as noted in the guidelines, marijuana has potent, toxic, addictive or abuse potential. (Tr.-1915-1916, l. 11-22, 1-

2; G-92A, pg. 22)

111. Dr. Voth testified on cross-examination that he prescribed narcotic drugs (opiate derivative medications used to treat pain) in his practice, and he acknowledged that such drugs can be abused and cause dependency. (Tr.-1950, l. 8-12; Tr.-1951-1952, l. 17-22, 1-5) Dr. Voth also noted that he used benzodiazepines, which are sedatives and can be addictive, in his practice. (Tr.-1952-1953, l. 7-22, 1-19)

112. During cross-examination, Dr. Voth agreed that he was opposed to legalizing marijuana as "medicine," and indicated that the legalization movement used "medical" marijuana as a "stalking horse." (Tr.-1966-1967, l. 12-22, 1-18)

113. However, during re-direct examination, Dr. Voth explained that his opposition to marijuana legalization was "the gaining of legal status of leaf marijuana, in other words, that it would be a substance that people could smoke at will, just for recreation or whatever purpose they chose." (Tr.-1968, l. 7-13)

114. Dr. Voth even published an article, which gave advice on how guidelines for "medical" marijuana for those states that have passed such "medical" marijuana laws. (Tr.-1969-1970, l. 14-22, 1-14)

115. Dr. Voth also testified that he is very supportive of research into the potential medical uses of marijuana's cannabinoids and individual components. (Tr.-1970, l. 15-20)

116. Although Dr. Voth was very enthusiastic about various cannabinoids use as potential medicine, he was concerned that the issue was driven by the marijuana legalization culture; Dr. Voth indicated that he would just as opposed if someone proposed tobacco for weight loss especially if it were the tobacco industry that was behind it. (Tr.-1970-1971, l. 21-22, 1-22) Dr. Voth noted that all the state ballot issues were an "end-run" to

circumvent the FDA process. (Tr.-1972-1973, l. 15-22, 1-2)

(e) **Testimony of Mahmoud ElSohly, Ph. D.**

117. Mahmoud ElSohly, Ph. D. (Dr. ElSohly) is a research professor at the National Center for Natural Products Research, Research Institute of Pharmaceutical Sciences, School of Pharmacy, University of Mississippi. (Hereinafter "Research Institute.") (Tr.-1130-1131, 14-22, 1-4) Dr. ElSohly has worked at the Research Institute since 1976. (Tr.-1130-1131, l. 13-22, 1-2) He is also the director of his own private laboratory, which is an analytic forensic laboratory located in Oxford, Mississippi. *Id.* Dr. ElSohly testified that there is quite a bit of collaboration between the Research Institute and his own forensic laboratory. (Tr.-1138, l. 20-22) Dr. ElSohly has a number of co-investigators, co-workers and associates in his endeavors with the study of marijuana. (Tr.-1139, l. 1-8)

118. One of the primary drugs that Dr. ElSohly has worked with for many years is marijuana. (Tr.-1131, l. 5-12)

119. Prior to working at the Research Institute, Dr. ElSohly was a teaching assistant at the University of Pittsburgh, School of Pharmacy, and he was a teaching assistant at the Department of Pharmacognosy (science of natural or herbal products), University of Cairo.. (Tr.-1132, l. 3-22)

120. Dr. ElSohly's extensive curriculum vitae highlighted, *inter alia*, the following: a B.S. in pharmacy from the University of Cairo, a Masters in pharmacy and pharmaceutical sciences from the University of Cairo, a Ph. D. in pharmacy/pharmacognosy from the University of Pittsburgh; and 200 related academic publications, many of which deal with natural products that emanate from marijuana. (Tr.-1134, l. 2 to 1136, l. 15; G-93)

121. Dr. ElSohly mainly examines the chemistry of marijuana, which includes extractions, isolation of different components, analysis of plant material (including marijuana grown at the Research Institute and confiscated marijuana) and analysis of illicit marijuana. (Tr.-1136-1137, l. 16-22, 1-12) Dr. ElSohly developed procedures for extraction (using the solvent ethanol) and isolation of tetrahydrocannibinol (THC), which is the main component of the marijuana plant; he also developed other processes for manufacturing or synthesizing other cannabinoids that have other biological activities. (Tr.-1137-1138, l. 13-22, 1-17; Tr.-1143-1144, l. 11-22, 1-13) To these ends, Dr. ElSohly has been involved in cultivating marijuana for about 29 years. (Tr.-1150, l. 17-22)

122. Dr. ElSohly explained that the Research Institute was initially registered with DEA to work with marijuana in 1968. (Tr.-1151-1152, l. 20-22, 1-7) From 1976 to 1980, Dr. ElSohly was the co-project director for the Research Institute. (Tr.-1156, l. 20-22) Dr. ElSohly became the Research Institute Director in 1980 (Tr.-1152, l. 8-20)

123. The Research Institute at the University of Mississippi had a DEA analytical laboratory registration that allowed the Research Institute to cultivate, research, conduct analytical work and distribute marijuana to researchers on behalf of NIDA. (Tr.-1152-1153, l. 21-22, 1-15)

124. The Research Institute contracts with NIDA to supply marijuana to researchers; the contract is renewed through competitive bids and the announcement for bids on the NIDA contract is published in the Federal Register. (Tr.-1154, l. 3-22; Tr.- 155, l. 1-13; G-12, pg. 2, § B.1; G-13, pg. 2, § B.1) NIDA pays the Research Institute for the marijuana on a cost reimbursable basis. *Id.* The bidders are not disclosed so that Dr. ElSohly would not be aware who other competing bidders are, if any.

(Tr.-1157, l. 8-20)

125. Dr. ElSohly supplied the enormous amount of information required by NIDA in order to bid on the NIDA contracts of 1999 and the current (2005) contract, and the Research Institute was awarded both contracts. (Tr.-1216, l. 11 to Tr.-1218, l. 3)

126. Researchers do not pay if they are operating under a Government grant; otherwise, the researchers pay a cost at reimbursement. (Tr.-1212-1213, l. 1-22, 1-4) The clinical researchers for the Center for Medicinal Cannabis Research (CMCR) pay for the NIDA marijuana at a cost reimbursement basis in the manner described by Dr. ElSohly (Tr.-1213-1214, l. 20-22, 1-6)

127. The NIDA contracting officer sets the price for the researchers to pay, and the Research institute is not involved in setting the prices. (Tr.-1213, l. 5-19) The institute makes no profit on the sale of regulated marijuana. *Id.*

128. Dr. ElSohly, in his capacity as Research Institute Project Director, is responsible for submitting the institute's bid to NIDA. (Tr.-1157, l. 1-17) As the director, Dr. ElSohly is responsible for obtaining the required DEA registrations, complying with all applicable laws including DEA laws, communicating with NIDA and DEA about the relevant scientific and legal aspects of the institute and supervises the growing, harvesting, potency monitoring, extraction analysis from the plant material and the isolation of the various components from the marijuana plants. (Tr.-1157-1158, l. 21-22, 1-19)

129. The NIDA contract was subject to renewal every three years, and the contract allows the Government (NIDA) to determine when or whether marijuana should be cultivated. (Tr.-1155-1156, l. 14-22, 1-3)

130. Starting in November 1999, NIDA changed the contract from a three

year cycle to a five year cycle, i.e., the bidding on the contract is now on a five year cycle. (Tr.- 1156, l. 4-7) Although the 1999 contract was set to expire in November 2004, it was extended until March 5, 2005, so that the new contract could be put in place. (Tr.-1159-1160, l. 16-22, 1-4) Dr. ElSohly submitted a bid to NIDA on behalf of the Research Institute, and NIDA awarded the contract to the institute as of March 2005 to March 2010. (Tr.-160, l. 5-19)

131. The NIDA contract has two subcontractors, one that supplies the security and the other, the Research Triangle Institute (RTI), located in North Carolina that processes the marijuana into cigarettes for use by research subjects. (Tr.-1161-1162, 18-22, 1-7) More specifically, RTI conducts analysis, certifies, distributes and generally takes care of sending the marijuana cigarettes to the researchers. (Tr.-1162-1163, l. 8-22, 1-8; G-12; G-13)

132. The Research Institute is apprised through NIDA and the researchers of what marijuana is needed for the researchers; the Research Institute fills the order by sending the bulk to RTI, and RTI then rolls the marijuana into cigarettes and ships the cigarettes to the researchers. (Tr.-1167-1168, l. 7-22, 1-8; Tr.-1168-1169, l. 21-22, 1-9) When RTI sends the cigarettes to the researchers, it sends directions to the researchers on how to store the marijuana and how to handle it. (Tr.-1168, l. 9-20)

133. The Research Institute has the ability to make marijuana cigarettes for researchers (which is an elaborate procedure including blending of various dried materials) when the cigarettes are needed on an expedited basis; in fact, the institute sent cigarettes of 8% potency to a researcher in California on this basis. (Tr.-1169-1170, l. 10-22, 1; Tr.-1202-1203, l. 17-22, 1; Tr.-1263-1264, l. 10-22, 1-6) Another reason that the

Research Institute filled this order, instead of RTI, is that higher potency marijuana is sticky and could "gum up" a cigarette rolling machine. (Tr.-1170, l. 5-19; Tr.-1226-1227, l. 12-22, 1)

134. Both the 1999 contract and the current (2005) contract require that the Research Institute cultivate marijuana on outdoor plots of $1^{1/2}$, 6 or 12 acres, the Research Institute has a secured 12 acre plot of land on which marijuana may be cultivated. (Tr.-1165, l. 5-22; Tr.- 1174, l. 12-22; G-12, pg. 2, § 2.B.(2)(b)) Under both contracts, NIDA must choose which option (in terms of the three acreage options). (Tr.-1166, l. 1-16) If the Government chooses to exercise or expand a growth option for a particular year, it will reimburse the institute on a cost basis for the increased cultivation. (Tr.-1172-1173, l. 20-22, 1-4) The Research Institute varies its cultivation techniques in order to obtain various potencies. *Id.*

135. NIDA also pays the Research Institute on a cost reimbursable basis for testing, analysis, research components isolation, the paraquat analysis, re-analysis of the current stock, inventorying the plant material, studies of the plant material and other activities outlined in the statement of work in the NIDA contracts. (Tr.-1173-1174, l. 5-22, 1-5)

136. Both the 1999 and current (2005) contracts require the institute to cultivate high potency marijuana, i.e., more than 3 to 4%; this potency was produced under the 1999 contract. (Tr.-1166-1167, l. 17-22, 1-5) The institute has been able to harvest, and have the stock and supply as high as 14%. (Tr.-1166-1167, l. 21-22, 1-6) For bulk marijuana, the institute has a range of potency that goes as high as 14%, and on a smaller scale can produce marijuana with a potency up to 20%. (Tr.-1203, l. 6 to 1204, l. 1)

137. The Research Institute has not produced high THC content

marijuana on a large scale yet because there is no demand for it at this time. (Tr.-1204, l. 2-19) But the institute is capable of providing to researchers any potency that is required by the researchers. (Tr.-1609, l. 9-21)

138. Statistics provided by RTI in regard to the number and potency of the cigarettes it produced, demonstrated that in April 2003, RTI produced 65,400 cigarettes of 6.34% THC potency. (G-27, pg. 2, last entry)

139. The Research Institute will supply bulk marijuana to researchers directly if the researchers want to roll their own cigarettes for the research subjects. (Tr.-1204-1205, l. 20-22, 1-15)

140. Cultivating marijuana outdoors depends on the geographical location, but in Mississippi the crop is planted about mid-April and can be harvested anywhere from September until as late as November. (Tr.-1205-1206, l. 16-22, 1-10) Marijuana is not sensitive to a light frost but can be adversely affected by temperatures of 25° or less. (Tr.-1206, l. 11-18)

141. Dr. ElSohly noted the obvious limitation of indoor marijuana cultivation, i.e. the limited cultivation capacity; however, the Research Institute could expand its indoor facility if need be. (Tr.-1245-1246, l. 11-22, 1-12)

142. The Research Institute indoor facility has the advantage of altering the growing season whenever it wants; *sensimilla* (seedless) marijuana can be produced in the indoor facility up to 20% THC; and marijuana is cultivated using hydrophonics (growing in just liquids) only in the indoor facility. (Tr.-1246, l. 2 to 1248, l. 9) The institute has not grown any indoor marijuana for NIDA. (Tr.-1459, l. 19-20)

143. However, the majority of the Research Institute's marijuana is grown outdoors; the indoor facility produces up to 10 kilograms a year, while

the outdoor facility produces in 100s of kilograms a year. (Tr.-1246-1247, l. 18-22, 1-12; Tr.-1248, l. 10-18)

144. Dr. ElSohly explained several methods of cultivating marijuana plants in order to harvest marijuana at specified potencies. (Tr.-1198, l. 2 to 1200, l. 14) One method is vegetative propagation whereby only the female part of the marijuana plant is replanted so that the next crop would be solely female plants. (Tr.-1242-1243, l. 18-22, 1-15) Another method is micro propagation whereby a very small amount of marijuana genetic material to develop specialized small plants that can be transferred to the indoor hydrophonics' section; this method allows a genetic material to be developed for specific purposes. (Tr.-1258-1259, l. 10-22, 1-10)

145. Dr. ElSohly noted that under the 1999 contract, the Government exercised the option for the Research Institute to produce 50,000 low THC cigarettes, 50,000 high THC cigarettes and 50,000 marijuana placebo cigarettes. (Tr.-1175, 1-21; G-12, pg. 2 § B(2)(b))

146. Dr. ElSohly testified that the last time NIDA required the Research Institute to grow a crop was for the years 2001-2002; NIDA may require the institute to grow a crop for the next Spring. (Tr.-1458-1459, l. 12-22, 1-8)

147. Dr. ElSohly explained that "THC" in the contracts referred to the potency of Delta 9 THC. (Tr.-1175-1176, l. 22, 1-7; Tr.-1264, l. 7-13) He also explained that placebo is faux marijuana. (Tr.-1180-1181, l. 9-22, 1-11) RTI rolls the placebo marijuana into cigarettes. (Tr.-1181-1182, l. 12-21, 1-12)

148. Initially, the Research Institute obtained marijuana seeds from abroad to start its marijuana crops, but now it uses its own seeds but still imports seeds as well. (Tr.-1255, l. 4-21; Tr.-1256-1257, l. 15-22, 1-11)

149. The last outdoor marijuana crop that was harvested was for the 2001-2002 season; the Research Institute has a large inventory covering all ranges of any material that researchers would need and if there are any needs outside of the range in the existing inventory such needs could be fulfilled by the indoor facility. (Tr.-1253-1254, l. 11-22, 1-3) Outdoors, the institute is capable of producing up to 15% THC potency. (Tr.-1254, l. 4-17) The outdoor crops are capable of producing 50 to 100 kilograms of marijuana with potencies of 10% to 13%. (Tr.-1254-1255, l. 18-22, 1-3)

150. Marijuana harvesting can be accomplished by cutting the whole plant at the base or harvesting at the top of the buds; female plants can be placed in trays and then into a dryer set to a certain moisture content. (Tr.-1260, l. 1-17) The plants then are removed from the dryer, manicured and then placed in a deseeding machine. *Id.*

151. The marijuana's potency then is determined by a gas chromatography process. (Tr.-1260-1261, l. 18-22, 1-8) Bulk marijuana is stored in drums; marijuana at 5% or less potency is stored in vaults without refrigeration but higher potency marijuana is stored in freezers to preserve potency. (Tr.-1261-1262, l. 5-22, 1-16) Dr. ElSohly explained that marijuana can be stored up to five days without any significant potent loss. (Tr.-1270, l. 13-22) High potency can be preserved by storing it in refrigerators of temperatures down to 20° and the longer it needs to be stored, the lower the temperature should be. (Tr.-1268, l. 13-20)

152. Dr. ElSohly explained that placebo marijuana cigarettes are used by research patients who are not informed if they are smoking placebo, low potency or high potency marijuana; this blinded research is done so researchers can measure actual to perceived effect of THC. (Tr.-1182-

1183, l. 13-22, 1-18)

153. Under both contracts, Dr. ElSohly is required to do analysis of marijuana samples that are seized or obtained by law enforcement; although the contract requires a 100 samples a month to be examined as a minimum, the institute actually analyzes 2,000 to 4,000 a year, and these analyses exceeds what is required by the contracts because the analysis included potency determinations. (Tr.-1176, l. 8 to 1180, l. 8; G-12, pg. 2, § B(1)) Through this testing, the Research Institute has traced the increase of potency of "street" marijuana and shared this information with the Office of National Drug Control Policy (ONDCP). (Tr.-1248, l. 19 to 1253, l. 1)

154. Dr. ElSohly explained, however, that NIDA would not necessarily deny the contract because the applicant would not want to analyze confiscated marijuana samples; the applicant could arrange for this provision to be subcontracted. (Tr.-1444-1445, l. 11-22, 1-10)

155. Dr. ElSohly explained that cannabinoids are natural components that only exist naturally in the cannabis plant; they contain 21 carbons. (Tr.-1140-1141, l. 17-22, 1-14) There are derivatives and synthetic analogs of these cannabinoids; but any compounds that are made to mimic the natural compounds are referred to as cannabinoids. (Tr.-1141, l. 9-12)

156. Both NIDA contracts required that the Research Institute perform extractions from marijuana plants and for developing new methods for growing low-THC content and placebo marijuana. (Tr.-1187, l. 4-22) Since experienced users can detect placebo marijuana from actual marijuana when smoking, the institute is in the process of developing a placebo marijuana that will keep all components in the marijuana except THC so that the placebo will not be detected when smoked. (Tr.-1187, l. 4 to 1189, l. 1)

157. Dr. ElSohly explained that the Research Institute isolates some of the 400 or 500 constituents in marijuana and that it is a very elaborate process to isolate or purify one component of marijuana. (Tr.-1224-1225, l. 9-22, 1-13; G-13, pg. 6, § 1(f))

158. Under the current contract, the Research Institute is required to and does isolate tetrahhydrocannabinol, a degradation component in marijuana that increases as the marijuana ages, from the marijuana plant; the institute also isolates cannabidiol (another component that varies with the variety of the marijuana plant) from the marijuana plant. (Tr.-1227, l. 10 to 1230, l. 3; G-13, pg. 7, ¶ 8) The institute is also in the process of producing one kilogram of pure THC as a standard and in the process of producing 100 grams of cannabinol and cannabidiol as a standard. (Tr.-1229, l. 3-8; Tr.-1230, l. 5-17; Tr.-1230-1231, l. 18-22, 1-3; Tr.-1231, l.5-18)

159. Most of the marijuana in stock at the Research Institutes is high in THC and low in cannabidiol; however, the institute does have other variations in its marijuana that could be placed into cigarettes if there is a need. (Tr.- 1497, l. 9-22) The institute has supplied marijuana that has ranged from low to medium cannabidiol. (Tr.-1448, l. 1-16) Dr. ElSohly testified that the institute has "maybe 100 different containers of different plant materials, and depending on the plants were those materials are harvested from, you can have a different cannabinoid iteration, and if you take all of these and blend them together, you would end up with the average that I'm talking about." (Tr.-1449-1450, l.8-22, 1-4)

160. The Research Institute also has two methods to produce *sensimilla*, seedless marijuana that is produced under the authority of both the 1999 and 2005 (current) contract. (Tr.-1189, l. 7 to 1193, l. 2) *Sensimilla* is

produced for its very high potency, which can range from 15% to 24% or even greater. (Tr.-1193-1194, 10-22, 1-4)

161. Under the current contract, the Research Institute performs triplicate analysis of a sampling on each marijuana harvest, which means that three samples from the same source are averaged in order to obtain a more accurate figure of the plant material's potency. (Tr.-1194, l. 19 to 1196, l. 3; G-13, pg. 6, § B.(1)(b))

162. The current contract also requires the Research Institute to develop and produce standardized marijuana with a range of specified THC potencies so that RTI can produce cigarettes with a range of specified potencies. (Tr.-1196, l. 4 to 1198, l. 1)

163. Dr. ElSohly explained that it is necessary to add moisture to the marijuana cigarettes to prevent loss of potency. (Tr.-1200-1201, l. 15-22, 1-12) The Research Institute has storage capacity at temperatures all the way to -20° in order to prevent potency degradation. (Tr.-1206, l. 11-18)

164. The Research Institute conducts stability studies on marijuana and stores the marijuana at various temperatures to make such determinations. (Tr.-1210-1211, l. 9-22, 1-10) The institute conducts these studies on bulk marijuana and some cigarettes while RTI conducts such studies on most of the cigarettes. (Tr.-1211, l. 11-22)

165. The Research Institute does have a Dug Master File (DMF), which was submitted to the FDA; this file describes all processes, procedures, qualities, validations, analytical data and the manufacturing process for producing marijuana. (Tr.-1208-1209, l. 17-22, 1-17) For marijuana, the DMF would include the cultivation process, harvesting, drying, de-seeding, analysis and validation of processes, validation of equipment used, quality control procedures, quality assurance procedures, stability

studies, and qualifications of the individuals involved. (Tr.-1209, l. 6-17)

166. The DMF in place for the Research Institute is submitted by NIDA and not by the institute or RTI. (tr.-1209, l. 18-21) NIDA is the owner of the DMF and would be the agency to give anyone permission to reference the DMF. (Tr.-1209-1210, l. 21-22, 1-6)

167. But if another manufacturer wants to produce marijuana similar to what the Research Institute does, it would have to develop its own DMF; the DMF is very specific to the product. (Tr.-1210, l. 5-8)

168. However, Dr. ElSohly indicated that if a pharmaceutical company wants to develop a marijuana extract product, Dr. ElSohly could seek permission from the FDA to allow that company access to the DMF of the Research Institute. (Tr.-1537-1538, l. 2-22, 1-6)

169. Dr. ElSohly also explained that if smoked marijuana were ever approved as a prescription medicine, such a product would have to have its own DMF, which would have to be approved by the FDA. (Tr.-1564-1565, l. 9-22, 1-16)

170. THC is the main active cannabinoid although there are another 65 cannabinoids contained in the marijuana plant that do not have the same psychological activity that THC has. (Tr.-1141-1142, l. 15-22, 1-7; Tr.-1142, l. 18-21) Most pharmacological activities ascribed to the cannabis plant could be accounted for by THC activity although other components might contribute to the overall activity of the plant. (Tr.-1142-1143, l. 22, 1-10) There are several THC's in marijuana, and they include THC Delta 6, 7, 8, 9 and 18A, but when one refers to THC it usually is in reference to THC Delta 9. (Tr.-1146-1147, l. 16-22, 1-3)

171. Potency refers to the concentration of THC in the plant material, i.e. the higher the THC concentration, the higher the potency. (Tr.-1148-

1149, l. 15-22, 1-7) Yield refers to the amount of usable material derived from cultivated plants; cultivation varies based upon whether the cultivation is indoors or outdoors, the growth cycle, what part of the country the marijuana is grown, and what kind of plant material. (Tr.-1149-1150, l. 10-22, 1-14) Usable material means smokeable material, which does not include seeds, stocks or roots but does include the actual leaves and buds. (Tr.-1150, l. 14-16)

172. Dr. ElSohly developed a "fingerprinting" program, which identifies marijuana based on similar characteristics of plants so that such plants can be grouped by region; in other words, if Dr. ElSohly receives confiscated marijuana, he can pinpoint where the marijuana was grown based upon its unique regional characteristics. (Tr.-1144, l. 14 to 1146, l. 9)

173. Dr. ElSohly has testified as an expert in marijuana about its potency, yield, analysis and identification of marijuana and marijuana extracts; Dr. ElSohly testified mostly in criminal proceedings and has testified on behalf of the Government and the defense. (Tr.-1147-1148, l. 1-22, 1-14)

174. Dr. ElSohly was qualified by the ALJ as an expert in the cultivation and research of marijuana. (Tr.-1151, l. 12-18)

175. Dr. ElSohly acknowledged receiving correspondence from Dr. Doblin, in which Dr. Doblin sought to have the Research Institute supply marijuana to a researcher, Dr. Donald Abrams, but Dr. ElSohly could not recall his response. (Tr.-1236, l. 7-21; R-28; R-29; R-32) But Dr. ElSohly explained that he could not have supplied the marijuana to Dr. Abrams because such a transaction would have to be approved by NIDA according to the contract between NIDA and the Research Institute. (Tr.-1236-1237, l. 22, 1-16)

176. For the same reason, Dr. ElSohly declined to test "Buyers' Club" marijuana that Dr. Doblin wanted to provide to the Research Institute for testing. (Tr.-1237-1238, l. 16-22, 1-13) However, a representative of the National Organization for the Reform of Marijuana Laws (NORML) arranged to have a DEA registered laboratory send a "Buyers' Club" marijuana sample to Dr. ElSohly who analyzed the sample under his own private DEA analytical laboratory DEA registration. (Tr.-1238-1239, l. 14-22, 1-21)

177. Dr. ElSohly testified that he received no formal complaints from researchers but did note that he found out that a CMCR researcher noted that NIDA marijuana sent at 8% potency was analyzed at over 7% but less than 8% potency. (Tr.-1274, l. 19 to 1276, l. 14; Tr.-1279, l. 4-17) The topic was mentioned during a phone call from a CMCR representative to Dr. ElSohly about one year ago, but the CMCR representative did not ask Dr. ElSohly to send another batch. (Tr.-1278-1279, l. 20-22, 1-20) No other person from CMCR asked that the Research Institute replace the marijuana sent under the "8%" potency designation. (Tr.-1279-1280, l. 21-22, 1-18)

178. Dr. ElSohly testified that this order was placed and made for an 8% potency but tested for 7.4% potency or close to that amount; he further explained that marijuana potency is made within a range as opposed to an exact amount. (Tr.-1276-1277, l. 17-22, 1-18) He explained that a variability in potency of plus or minus 20% is standard and accepted so that an acceptable range for 8% potency would be between 6.4% and 9.6%. (Tr.-1293, l. 21 to 1295, l. 1)

179. Dr. ElSohly further explained that the Research Institute's standard is plus or minus 10% so that an acceptable range for an 8% batch would be 7.2% to 8.8%. *Id.* (Note: The transcript indicates Dr. ElSohly stated

6.2%. (Tr.-1294, l. 18) The Government noted in the corrections that Dr. ElSohly testified "7.2%" or that Dr. ElSohly inadvertently testified "6.2%" when he meant "7.2%.") He noted that within the same batch, some cigarettes would be closer to an exact 8% than other. (Tr.-1295, l. 2-8)

180. The variation was not significant enough to scratch the initial batch made and start again. (Tr.-1277, l. 14-18)

181. Dr. ElSohly noted that the CMCR researcher actually used the batch sent to him by the Research Institute and the research subjects could not tolerate the potency of marijuana even though the potency was slightly less than the 8% requested. (Tr.-1280-1281, l. 11-22, 1-8) In fact, CMCR ended up requesting a 6% batch for the study since the research subjects could not tolerate the 7% to 8% potency. (Tr.-1280-1281, l. 19-22, 1-8)

182. In one of DEA's trip reports that summarized a DEA interview of CMCR researcher Dr. Donald Abrams, the issue of the "8%" batch was noted by Dr. Abrams. (Tr.-1286, l. 9 to 1288, l. 1; G-17, pg. 6) Dr. ElSohly confirmed that Dr. Abrams' remarks in the DEA trip report pertained to the same issue that he discussed with the CMCR representative over the phone. *Id.* (Dr. Abrams trip report indicated that the Research Institute had been "very responsive.") (Tr.-1288, l. 2-13; G-17, pg. 6)

183. Dr. ElSohly commented on another issue set forth in the same CMCR trip report; the comment indicated that some of the patients reported that their marijuana cigarettes were harsh. (Tr.-1288-1289, 14-22, 1-7; G-17, pg. 7, ¶ 14) Dr. ElSohly never received any formal complaints concerning this trip report comment, but he noted that he heard complaints that placebo marijuana was harsh, and he explained

that placebo cigarettes would have to be harsh since all of the marijuana components had been removed. (Tr.-1289-1290, l. 8-22, 1-2)

184. Dr. ElSohly had heard informal complaints about the "harshness" from Dr. Abrams about five or six years ago when he talked to Dr. Abrams at a conference they both were attending. (Tr.-1291, l. 1-12) But Dr. Abrams never followed-up on these comments by requesting that the Research Institute take any action. (Tr.-1291, l. 13-22) Nor did Dr. Abrams indicate to Dr. ElSohly that his (Dr. Abrams') research was curtailed based upon Dr. Abrams' informal complaints. (Tr.-1292, l. 1-5)

185. From the comment, Dr. ElSohly could not tell which patients complained or if such complaining patients were commenting about placebo cigarettes. (Tr.-1290, 3-9)

186. Dr. ElSohly also noted that some humidity would be lost over time due to storage but that problem was not at all related to the nature of the marijuana itself. (Tr.-1290, l. 10-22)

187. Dr. ElSohly was referred to another trip report, which summarized comments by CMCR researchers pertaining to the marijuana supplied by the Research Institute through NIDA.; this comment noted that patients complained about the 'harshness" of some of the cigarettes. (Tr.-1295-1296, l. 21-22, 1-11; G-18, pg. 7, ¶ 14) Dr. ElSohly responded that he never received any formal complaints about this issue, that, again, he could not determine if the complaints related to the placebo and that the complaint referred to only one of ten patients. (Tr.-1296, l. 12-22)

188. Another researcher mentioned in the CMCR trip report that two or three research subjects dropped out of the study because the marijuana was harsh. (Tr.-1320, l. 1-21; G-21, pg. 7-8, ¶ 15) Dr. ElSohly again testified that he never received any formal complaints about this issue,

he did not know if the harshness referred to placebo, and he opined that 92% of the patients remained in the study so that there was no apparent impeding of this particular trial. (Tr.-1320, l. 1 to 1322, l. 7)

189. Dr. ElSohly testified that he never received any formal complaints about the institute's marijuana having too many sticks and stems. (Tr.-1297-1298, l. 19-22, 1-6) Again, Dr. Abrams made remarks to this effect when he and Dr. ElSohly talked informally at the same conference of four or five years ago when Dr. Abrams talked about the problem the "harshness." (Tr.-1298, l. 7-16)

190. Dr. ElSohly noted that the Research Institute early on had deseeding machines, which rendered the marijuana to very fine (minute) particles. (Tr.-1298-1299, l. 17-22, 1- 10; Tr.-1303, l. 6-14; Tr.-1304, l. 10-13) RTI informed the institute that the marijuana was too fine to be rolled, so RTI took on the job of deseeding. (Tr.-1299, l. 11-19) Thus, around 2001 to 2002, the institute's marijuana was very rough with stems and sticks, which were removed for cigarette production by RTI. (Tr.-1299-1300, l. 20-22, 1-10)

191. In 2001, the Research Institute worked with a company in Canada to design a special deseeding machine; the machine was placed into operation in 2001 and it is able to remove all stems, seeds and the heavy particles so that RTI does not have to process the marijuana other then blending and humidifying. (Tr.-1301, l. 2-15)

192. Dr. ElSohly explained that any excessive seeds or stems left in the marijuana would puncture the fine cigarette paper as the marijuana is being rolled into the cigarettes by the RTI machine. (Tr.-1303-1304, l. 15-22, 1-9)

193. Dr. ElSohly was referred to pictures of NIDA marijuana, and these pictures, which were contained in an article authored by Ethan Russo,

M.D., show a number of sticks and stems purportedly removed from a NIDA (Research Institute) cigarette. (Tr.-1305, l. 6-21; R-19, pg. 49-50)

194. Dr. ElSohly commented that the pictured seeds and stems appeared in the pictures to be 1 to 1½ times the size of the actual size and that had the stems and seeds in the pictures been inside a NIDA marijuana cigarette, the cigarette paper would have been punctured. (Tr.-1305, l. 22 to 1308, l. 3) Based upon the pictures, Dr. ElSohly believed the particles would be too large to be rolled into a cigarette. (Tr.-1603, l. 1-19) He also testified on cross-examination that the pictures appeared to be from the raw material rather than cigarettes. (Tr.-1599, l. 10-21)

195. Dr. ElSohly was referred to another CMCR trip report comment from Dr. Abrams who commented that the marijuana cigarette was nicely rolled "but that there is a loss of material in the case from dropping out of the cigarette as a result of the pre-thaw process." (Tr.-1308-1309, l. 19-22, 1-5; Tr.-1309-1310, l. 18-22, 1; G-21, pg. 6, ¶ 11)

196. In reference to the latter comment, Dr. ElSohly explained that he did not consider the comment a complaint because the cigarettes were made out of dried leaves of plant material that is not shredded like tobacco so that one would expect some of the material would fall off the top when there are no seeds on top. (Tr.-1310, l. 21 to 1312, l. 7) Dr. ElSohly further explained that the cigarettes are packaged by inserting them vertically into a can (300 per can) and no matter how well packaged, some marijuana will fall off the top of the cigarette to the bottom of the can. (Tr.-1311-1312, l. 12-22, 1-19) He also noted that cigarettes processed in this manner cannot be hand rolled to tie up the ends. (Tr.-1312, l. 14-17)

197. Dr. ElSohly addressed the comment, noted in the CMCR trip report

by Dr. Abrams, which indicated that the NIDA marijuana should mimic that which is found in the San Francisco area. (Tr.-1312-1313, l. 21-22, 1-20; G-21, pg. 7, ¶ 13) Dr. ElSohly explained that there was no formal complaint in this regard and that the comment did not make sense in that [illicit] marijuana would vary considerably depending on what part of the country the marijuana came from. (Tr.-1313, l. 7-20; Tr.-1315-1316, l. 8-22, 1-8) Dr. ElSohly further explained that research that employs blind investigations must ensure uniformity in the marijuana and even the data on the marijuana potency varies throughout the State of California so that one could not even generalize by area or city. (Tr.-1317, l. 5-22; Tr.-1318-1319, l. 16-22, 1-15)

198. Dr. ElSohly was referred to another comment on a CMCR trip report; the comment indicated that the researcher would like to minimize the smoke that the patient ingests and maximize the amount of therapeutic THC. (Tr.-1322-1323, l. 8-22, 1-4; G-21, pg. 7, ¶ 13) Dr. ElSohly agreed that it would be best to limit the amount of smoking and even better to find alternative delivery systems. (Tr.-1323-1324, l. 5-22, 1-13)

199. Dr. ElSohly testified about a number of abstracts that described some of the unique features of all the Research Institutes' marijuana projects. Tr.-1325, l. 16 to 1330, l. 12; G-6; G-7; G-8)

200. Dr. ElSohly also testified about the patents he had obtained that were related to the Research Institute's and Dr. ElSohly's work with marijuana. (Tr.-1331, l. 19 to 1335, l. 14; G-67 through G-71)

201. Dr. ElSohly testified about the various registrations that the Research Institute and he had. (Tr.-1337, l. 8 to 1342, l. 15) The Research Institute had a DEA manufacturing registration based upon its contract with NIDA to supply researchers with marijuana. (Tr.-1337, l. 8-20; G-

76)

202. The University of Mississippi has a second DEA manufacturing registration to research and develop pharmaceutical products from marijuana extracts. (Tr.-1338, l. 10 to 1340, l. 4; G-75) Dr. ElSohly explained in his opinion that theoretically only one manufacturing registration would be required but that DEA wanted two separate registrations, one for the NIDA contract and the other for private pharmaceutical development. (Tr.-1353, l. 1-8; Tr.-1354, l. 12-22)

203. In 1999, the Research Institute entered into a Memorandum of Agreement (MOA) with the DEA. (G-78) The MOA required the institute to have a separate DEA registration so that the institute could develop a medicinal THC extract that would be delivered via a suppository. (Tr.-1462-1463, l. 16-22, 1-9; Tr.-1469-1470, l. 21-22, 1-5; Tr.-1495-1496, l. 4-22, 1-3; G-78, pg. 2, § III)

204. The MOA noted that the Single Convention on Narcotic Drugs, 1961, (Single Convention) prohibited private trade in cannabis, but that private trade was not prohibited for "cannabis preparations" and the THC extract would fall within the latter exception. (G-78, pg. 2-3)

205. The pharmaceutical company that the Research Institute was working with to develop this suppository product is Mallinckrodt. (Tr.-1464-1465, l. 19-22, 1-8; G-79) On June 15, 2005, DEA wrote the University of Mississippi. (G-79) The letter explained, *inter alia*, that if the Research Institute wanted to actually sell the extract to Mallinckrodt for product launch, then the institute would have to obtain another separate DEA manufacturing registration with DEA. (Tr.-1520-1521, l. 15-22, 1-15; G-79, ¶¶ 1, 10-11)

206. Dr. ElSohly noted that his project with Mallinckrodt did not involve plant material marijuana but extracted THC, and under these

circumstances there was a huge difference between the Mallinckrodt proposal and what Dr. Craker was seeking to do. (Tr.-1507, l. 4-12) The extract consists of cannabinoids but not the plant material. (Tr.-1609-1610, l. 22, 1-9)

207. Mallinckrodt's goal is to launch its marijuana THC extract product when the Marinol patent expires. (Tr.-1538, l. 8-17) However, if another pharmaceutical company wanted to purchase the THC extract from the Research Institute, it could do so. *Id.* But the purifying process for the THC extract is exclusive, so that if another company purchased the THC extract, it would have to develop its own purification process. (Tr.-1538-1539, l.18-22, 1-6)

208. The Research Institute does have a financial interest in producing THC extract for Mallinckrodt, and it is the only producer of THC extract for this purpose at this time. (Tr.-1541-1542, l. 4-22, 1-14)

209. Although Mallinckrodt is obligated to buy a certain amount of THC extract from the Research Institute, above that amount it is theoretically possible for Mallinckrodt to purchase the THC extract from another supplier. (Tr.-1543-1544, l. 8-22, 1-4)

210. Although Dr. ElSohly was not aware that a quota was required for an extract, DEA required the Research Institute to keep a quota for the extract that is prepared from the plant marijuana. (Tr.-1523-1524, l. 1-22, 1-10; Tr.-1525, l. 2-13)

211. Dr. ElSohly explained that it was not necessary for the institute to undergo any review from NIDA [via a review of a research protocol by the Public Health Service) in order to develop the THC extract in conjunction with Mallinckrodt because the institute was not using NIDA marijuana. (Tr.-1499-1500, l. 6-22, 1-18) (Dr. ElSohly explained that if a researcher is not capable of growing his or her own marijuana, but

wants to do research with marijuana, then that researcher must go through NIDA and have the protocol reviewed by the PHS. Tr.-1501-1502, l. 4-22, 1-2)

212. Dr. ElSohly further explained that if a person wants to prepare and distribute marijuana to a researcher, that person would need a DEA registration as a manufacturer. (Tr.-1504-1505, l. 11-22, 1-2)

213. Dr. ElSohly also testified that DEA separated the two manufacturing registrations because DEA believed that under the law, a DEA registrant could not distribute marijuana except under the NIDA contract. (Tr.-1355, l.1-22) Dr. ElSohly believed that the latter distinction was based upon what was set forth in the Single Convention, although he was reluctant to make legal interpretations. (Tr.-1356, l. 1-13)

214. The Research Institute has a DEA registration as an analytical laboratory. (Tr.-1340-1341, l. 5-22, 1-1-9; G-77) The Research Institute also has a DEA registration as a researcher, which permits the institute to research marijuana and its components. (Tr.-1341-1342, l. 18-22, 1-15)

(f) **Affidavit of Kenneth H. Davis, Jr. (Research Triangle Institute)**

215. Kenneth H. Davis, Jr., Senior Program Director, Bioanalytical Chemistry Center, Research Triangle Institute (RTI), Research Triangle Park, North Carolina, submitted an affidavit, admitted upon stipulation, about RTI's role in relation to the Research Center at the University of Mississippi. (G-97)

216. RTI was formed in 1958 and employs researchers who have degrees in over 130 disciplines. RTI has six DEA registrations: Schedules I-V manufacturing (including bulk), Schedule I-V distributor, Schedule I-V importer (including bulk), Schedule I-V exporter, Schedule I researcher, and Schedule II-V researcher. (G-97, pg. 1)

217. Since 1968, RTI has been involved in the NIDA Project by producing and distributing marijuana cigarettes to FDA/DEA/NIDA-approved researchers as well as to patients in the experimental use program. The bulk marijuana for rolling marijuana cigarettes has been supplied by the University of Mississippi (the Research Center) under contract with NIDA. Until 1999, NIDA contracted with both U. Miss. and RTI for services provided to the NIDA M Project. In 1999, NIDA commenced to award one five-year contract to U. Miss. U. Miss. in turn subcontracted with RTI for continuation of its participation in the NIDA M Project. (G-97, pg. 2, ¶ 1)

218. In 1976, RTI acquired the machine that RTI still uses to make marijuana cigarettes. RTI has gained technical expertise from the state's tobacco industry in order to make marijuana cigarettes. RTI, however, is faced with the dilemma of taking a sample of a plant (mostly leaves but some stems and seeds) of known concentration and producing cigarettes that cannot be distinguished from higher potency or zero potency marijuana cigarettes. (G-97, pg. 2, ¶ 2)

219. RTI receives barrels of manicured marijuana from U. Miss. at about an 11.2% humidity level. The marijuana is processed so that the marijuana reaches a 16% humidity level. It then is stored in a cold-room to keep it from losing moisture. The material is then fed through a hopper into a cigarette-rolling machine, which makes the cigarettes and feeds them to be packed in trays. When the machine runs optimally, it produces 800 to 1,000 cigarettes a minute. After the cigarettes are dried by fans and heaters, they are packed into cans; one can hold about 300 marijuana cigarettes. (G-97, pg. 2, ¶ 3)

220. A total of 32 batches of machine rolled marijuana cigarettes have been produced by RTI since the beginning of the NIDA Project. These

32 batches have been available for and used in legitimate scientific research since 1974, at NIDA's direction, and pursuant to contractual obligations between NIDA, the Research Center, and RTI. Production is governed by what NIDA needs and requests. (G-97, pg. 3, ¶ 2)

221. RTI also produces small batches of 100-500 hand rolled cigarettes for special studies. One such batch was rolled to satisfy a request from the Center for Medicinal Cannabis Research (CMCR) in San Diego, CA, which specified 8% THC. Plant material bearing that quantity of THC is sticky and thus more challenging for mechanical rolling. Recent consultations with expert machine operators have led RTI to believe that it could now produce machine rolled cigarettes at 8% THC if necessary. On occasion, a researcher requests RTI to ship bulk material to researchers. (G-97, pg. 3, ¶ 3)

222. The ability to develop higher potencies has been progressing. An 8% THC marijuana is currently available and 10% THC could be accessible as well. One of the challenges is about the stability of higher THC cigarettes. Quarterly stability studies and quality control analyses are performed on bulk marijuana and marijuana cigarettes. The studies include plant material stored at room temperature as well as plant material frozen and refrigerated. (G-97, pg. 4, ¶ 2)

223. The goal of RTI concerning the NIDA M Project is to develop and provide a cigarette product that is consistent and standardized to support needs as identified by NIDA. RTI acknowledged that over the past 20 years they have received comments through NIDA concerning the quality of the marijuana cigarettes, although they have not received any since a few months before July 2002. RTI found that some of the criticism was alleviated by RTI providing instructions on how to humidify the product so that the product was not as "harsh." (G-97, pg.

3, ¶ 4)

224. RTI also acknowledged that the Research Center added a machine in 2001, which grooms the marijuana plant material and removes the vast majority of seeds and stems. RTI said that initially the groomed material was too fine and that created a problem for the cigarette-rolling machine; tobacco strands are larger and longer and the machine was equipped to deal with larger plant material. Expert machine operators assisted RTI and those problems have been resolved. RTI has not received any recent complaints about seeds or stems in their finished products. (G-97, pg. 3-4)

225. To date, RTI has not received any requests for marijuana products other than plant material. They have, however, received inquiries. RTI has a willing research team that would be eager to work on other delivery forms. RTI would need to "tool up" and would certainly be able to do so. (G-97, pg. 4, ¶ 3)

(g) **Testimony of Matthew Strait**

226. Matthew Strait (Mr. Strait) is a Supervisory Physical Scientist, Office of Drug Control, Drug and Chemical Evaluation Section, in DEA; in this capacity, he also I the Unit Chief for the Quotas and the United Nations Reporting Unit. (Tr.-774-775, l. 19-22, 1-10; Tr.-776, l. 11-14) Mr. Strait has worked for DEA, Office of Drug Control, Drug and Chemical Evaluation Section, since 1999. (Tr.-776, l. 15-22) He has a Masters of Science Degree. (Tr.-777, l. 1-3)

227. His duties include working to set quotas for all manufacturers of Schedule I and II controlled substances, processing and coordinating all Schedule I controlled substance researchers, handling treaty obligations including providing statistical reports to the International Narcotics Control Board of the United Nations, and assisting other units in the

processing of applications including applications for bulk manufacturers of Schedule I and I controlled substances, and including import and export registration permits. (Tr.-775-776, l. 11-22,1)

228. Mr. Strait is familiar with DEA applications to register those who seek to manufacture (cultivate) controlled substances; part of his duties were working on Dr. Craker's application as of October 2002. (Tr.-777, l. 4-15)

229. Mr. Strait explained that on March 4, 2004, Frank Sapienza, then Chief of the DEA Office of Drug Control, Drug and Chemical Evaluation Section, sent a letter to Dr. Craker; Mr. Strait helped prepare this letter (Tr.-784-785, l. 5-22, 1-11; G-29)

230. The letter noted that Dr. Craker submitted the application because he believed he could provide a better quality or higher potency marijuana than that which was provided by NIDA [through the University of Mississippi's Research Institute]. (G-29, pg. 1) Mr. Sapienza's letter explained that, based upon contact with NIDA and some researchers, marijuana of 7% to 8% potency is available to NIDA and that a higher potency could be supplied if needed. *Id.* The letter also noted that "DEA continues to have international treaty and legal concerns regarding your application." *Id.*

231. Mr. Sapienza's letter also informed Dr. Craker that DEA received a letter from Dr. Ethan Russo, who complained about NIDA marijuana; Mr. Sapienza's letter responded that Dr. Russo was not a DEA registered researcher for marijuana and that DEA was not persuaded by his arguments. (R-29, pg. 2) The letter concluded by requesting that Dr. Craker "provide this office with any credible evidence to support your assessment of this issue." *Id.*

232. Mr. Strait testified that DEA decided to interview the CMCR clinical researchers who used NIDA marijuana, and to interview personnel from NIDA and the FDA. (Tr.-790-791, l. 9-22, 1) Mr. Strait was one of the DEA personnel tasked to interview the CMCR researchers, and when he conducted the interview he had a form questionnaire prepared for the interviews. (Tr.-792-793, l. 19-22, 1-19; Tr.-800, l. 11-19) All the CMCR researchers who were interviewed had a chance to look over the form for accuracy and change or edit comments as appropriate. (Tr.-804-805, l. 8-22, 1-3)

233. Commencing September 2003, Mr. Strait interviewed, either in person or by telephone, the following CMCR clinical researchers: Dr. Grant, Dr. Cory-Bloom, Dr. Wallace, Dr. Israelski, Dr. Ellis and Dr. Abrams. (Tr.-802, l. 18, to 805, l. 22; Tr.-826-827, l.12-22, 1; G-17)

234. Dr. Igor Grant, who was the head of the CMCR project, was the first person to be interview along with a number of CMCR administrators and staff. (Tr.-793-794, l. 20-22, 1-16; G-16) Before the questionnaire was completed for Dr. Grant, Dr. Grant explained the CMCR clinical research project. (Tr.-808, l. 15 to 810, l. 17) Specifically, Dr. Grant explained, *inter alia*, that CMCR was at Stage One, at which CMCR researchers gave their research subjects smoked marijuana. (Tr.-808-809, l. 15-22, 1-9; Tr.-810, 13-17)

235. Dr. Grant noted that marijuana provided to researchers ranged from potencies of 0% to approximately 8%. (G-16, pg. 2, ¶ 3b.) Dr. Grant explained that the amount of marijuana requested was "based on enrollment into the approved research protocols." (G-16, pg. 3, ¶ 4)

236. Dr. Grant noted that "NIDA has been reliable" and that NIDA has been "easy to work with and amicable to accommodating for the requirements of the study." (G-16, pg. 6, ¶ 14) He noted later that it

was difficult to obtain high potency marijuana at 6% to 8% potency but that NIDA was very accommodating in producing the high potency marijuana in a timely manner. (Tr.-9, G-16, pg. 9, ¶ 19)

237. Although Dr. Grant answered "N/A" to the question of whether there were any instances related to the supply of marijuana by NIDA, he made two other remarks in ¶ 14. (G-16, pg. 6, ¶ 14) He noted that "problems have been higher potency material due to range of potency [and] high product is hand rolled and this difficult to prepare." *Id.*; (g-16, pg. 12, ¶ 25) Later in the questionnaire, Dr. Grant (through comments made by CMCR administrator Heather Bentley) further explained that "the one area we might like to see more reliability on the strength of the medical marijuana cigarettes. We know this is difficult with the plant material but we were told that GW can guarantee with more certainty." G-16, pg. 9, ¶ 19; Tr.-819-820, l. 16-22, 1-9) Within this same comment it was noted: "They [CMCR] don't know if U. Miss. that..." *Id.*; Tr.-820, l. 10-14)

238. But even later in the questionnaire, Dr. Grant not that the potency of the marijuana cigarettes ranged from 0 to "...7-8%- was 8, but actually within a 20% range of the target doses." (G-16, pg. 15, ¶ 31) Although Dr. Grant answered "no" to the question of whether the potency was consistent, he added the following comment to this answer: "There is a variation along the target that NIDA ensures to be within." (Tr.-822-823, l. 16-22, 1-3; G-16, pg. 12, ¶ 25)

239. Dr. Grant noted that it was his impression that 8% "was the higher limit, perhaps future." (G-16, pg. 18)

240. Dr. Grant also noted that CMCR's future goals would include moving from smoked marijuana to other delivery systems. (G-16, pg. 8, ¶ 18)

241. Dr. Grant noted: "Did go to U. Miss and Dr. ElSohly to see old and new material. They receive the new material mostly devoid of seed and stems." (G-16, pg. 12, ¶ 27)

242. Dr. Grant noted that "occasionally" a patient complained of "harshness" of the marijuana that produced a cough. (G-16, pg. 13, ¶ 29; Tr.-824, l. 3-8) This comment also indicated: "Dr. Wallace has not experienced any problems from patients." *Id.*

243. Ronald Ellis, M.D., Ph.D., a CMCR clinical researcher also was interviewed and a questionnaire was filled out based upon his answers. (Tr.-828-829, l. 2-22, 1-3; R-17)

244. Dr. Ellis answered "no" to the question: "Is the potency of the current product consistent?" (R-17, pg. 6, ¶ 10) To this answer, he added the comment: "At least 2 shipments some variability in stated THC and the actual measured. They have been very responsive." *Id.*

245. Dr. Ellis noted in the questionnaire that some patients reported that the marijuana smoke was "harsh," and it was hard to finish the cigarette. (R-17, pg. 7, ¶ 14) Dr. Ellis also noted that most, if not all, of the patients were experienced cannabis users. *Id.* Dr. Ellis also noted that issues regarding the quality (pertaining to freshness) of the marijuana did not adversely impact his research and that just one patient was dropped from a study due to a cough. (G-17, pg. 7, ¶ 15)

246. When Dr. Ellis noted the range of potencies received for the CMCR research (1% to 8%), he noted that when the 8% batch was received, its tested potency was about 7%. (G-17, pg. 9, ¶ 16) Later on in the questionnaire, however, Dr. Ellis explained "potency has not been a limiting consideration" in response to the question, "[d]o you feel that it would be clinically important to evaluate the efficacy of a higher potency cigarette for your patient population?" (G-17, pg. 10, ¶ 19)

247. Jody Corey-Bloom, M.D., Ph.D., a CMCR clinical researcher also was interviewed and a questionnaire was filled out based upon her answers. (Tr.-836-837, l. 14-22, 1-4; G-18)

248. Dr. Corey-Bloom noted that one out of ten patients complained of the marijuana being "harsh" but she did not know if the patient was referring to a placebo cigarette or not. (R-18, pg. 7, ¶ 14) She also indicated that the potency she received was acceptable for the kinds of studies she was doing, but the potency she was using was 4%. (G-18, pg. 9, ¶¶ 16-17) She noted that it had been difficult to recruit patients because people are not smoking to the degree they used to, there was a lot of inclusion/exclusion criteria, and the time commitment. (G-18, pg. 12)

249. Dr. Corey-Bloom commented that she would "like to explore the envelope of concentrations to evaluate the 'more is better concept.'" (Tr.-992, l. 13-21; G-18, pg. 10, ¶ 19) Mr. Strait explained that the context of this remark was not seeking a higher potency for the present study but for future research. (Tr.-997, l. 1-10; G-18, pg. 10, ¶ 19)

250. Dennis M. Israelski, M.D., a CMCR clinical researcher also was interviewed and a questionnaire was filled out based upon his answers. (Tr.-843-844, l. 21-22, 1-22; G-19)

251. Dr. Israelski did not recall any patient ever complaining about the "freshness" of the marijuana. (G-19, pg. 7, ¶ 14)

252. Dr. Israelski was presented with a cursory news article from the San Mateo Times, dated January, 24, 2003. (Tr.-849-850, l. 2-22, 1-3; G-30A) This news article was attached to a letter, dated June 30, 2003, from Dr. Craker to then-chief of the DEA Chemical and Drug Section, Frank Sapienza. (G-30; G-30A) Dr. Craker's letter was to respond to Mr. Sapienza's letter of March 3, 2003 (G-29); Mr. Sapienza's letter

asked Dr. Craker to supply DEA with information of why a second supplier was needed, and Dr. Craker submitted this news article in response. (G-30; G-30A)

253. The news article made a general averment that the CMCR researchers were not satisfied with the quality of NIDA marijuana. (G-30A) Dr. Israelski noted that he never made any comments about the NIDA marijuana, that the article misrepresented his views and that he was so concerned about the San Mateo Time's article that he stopped reading the paper and considered writing a letter to the editor. (Tr.-849-850, l. 15-23, 1-3 G-19, pg. 12)

254. Dr. Israelski also referred to patient Phillip Alden who is quoted in the San Mateo Times article as being critical of the NIDA marijuana. (G-19, pg. 12) Dr. Israelski explained that a patient's perception of the quality is often times different that the researcher's perception. (Tr.-850-851, l. 4-22, 1) Dr. Israelski did not make an explicit comment about Phillip Alden's comment that the NIDA marijuana caused bronchitis, but Dr. Alden did state that he had wished he had the chance to prescreen Mr. Alden's response to the news reporter. (Tr.-851, l. 2-10; G-19, pg. 12)

255. Mark Wallace, M.D., a CMCR clinical researcher also was interviewed and a questionnaire was filled out based upon his answers. (Tr.-852-853, l. 8-22, 1-9; G-20)

256. Question number ten asked: "Is the potency of the current product consistent?" (G-20, pg. 6, ¶ 10) Dr. Wallace responded that the "product falls within the range specified ..." but also noted that other factors, such as how the product was consumed, would come into play in response to this question. (Tr.-855-856, l. 13-22, 1-10; G-20, pg. 6, ¶ 10)

257. None of his patient populations complained that the marijuana was not "fresh" even though Dr. Wallace described his patients as "occasional users." (G-20, pg. 7, ¶ 14)

258. Donald Abrams, M.D., a CMCR clinical researcher also was interviewed and a questionnaire was filled out based upon his answers. (Tr.-859, 4-21; G-21)

259. Dr. Abrams had five protocols for clinical marijuana research study. (G-21, pg. 1) One predated the CMCR program, and the last protocol listed, "Vaporization as a Smokeless Delivery System" was just approved at the State and Federal levels after Dr. Abrams questionnaire was completed. (*Id.*, Tr.-864, l. 6 to 866, l. 12)

260. Dr. Abrams answered "no" to question number ten: "Is the potency of the current product consistent?". (G-21, pg. 6, ¶ 10) Dr. Abrams stated that a study had been approved for 3.9% THC but that NIDA informed the potency had been downgraded to 3.5%. (G-21, pg. 6, ¶ 10 note)

261. Dr. Abrams noted that he noted no physical deformities in the appearance of the cigarettes and that they were nicely rolled. (G-21, pg. 6, ¶ 11) He did note that there was a loss of material in the can from dropping out of the cigarette as a result of the "freeze/thaw process" and that rolling the ends would prevent loss. *Id.*; Tr.-1041-1042, l. 21-22, 1-12)

262. Dr. Abrams answered "no" to question number 14: "Have any patients ever complained about the "freshness" of the marijuana?" (G-21, pg. 7, ¶ 14) In the comment section to this question Dr. Abrams noted: "There is a harshness which irritates the posterior + larynx, 'good marijuana' may cause coughing, but that is not due to harshness as other 'smooth' products may cause cough." *Id.* Dr. Abrams further

commented: "If you don't cough, you don't get off. .." *Id.* The latter comment was an adage used by some to explain the positive benefit of a cough, which is a different cough than that caused by harshness. *Id.* ; Tr.-862, l. 9-20)

263. Dr. Abrams answered "yes" to question number 13: "In your professional opinion, do any of the plant parts make the cigarettes unacceptable for your research?". (G-21, pg. 7, ¶ 13) Dr. Abrams, in the comment section, stated: "If the goal is to mimic that which is being consumed in the SF area, then it would seem inappropriate to have stems and seeds in them. Also, trying to minimize those components resulting from smoke that are harmful while at the same time 4 medicinal value of THC." *Id.*

264. Later in the questionnaire, Dr. Abrams reiterated that his research would want to use marijuana of potencies available on the street, i.e. potencies, according to MAPS data, that ranges from 8% to 12% potency. (Tr.-871-872, l. 6-22, 1-18; G-21, pg. 9, ¶ 17, pg. 10, ¶ 19)

265. Dr. Abrams noted that his patients were experienced marijuana users, i.e. not naïve patients who never used marijuana prior to becoming a patient in Dr. Abrams' CMCR research. (Tr.-875-876, l. 7-22, 1-21; G-21, pg. 10, ¶ 19) The ones who were less experienced users were likely to have "more dysphoric effects." *Id.*

266. Dr. Abrams indicated he had no problem recruiting patients and that only a few dropped out "due to harshness of cig." (Tr.-878-879, l. 3-22, 1-14; G-21, pg. 12) Dr. Abrams noted that a few patients, two out of twenty or twenty-one terminated from the study early due to "harshness." (Tr.-1045-1046, l. 19-22, 1-11; G-21, pg. 8, ¶ 15) Dr. Abrams noted specifically that a total of four patients out of fifty "have dropped out due to quality." *Id.*

267. Dr. John Polich, who is a clinical researcher that investigates the effects of smoking marijuana on the brain, also filled out the standard questionnaire, although he is not a CMCR researcher. (Tr.-881-882, l. 1-22, 1-15; G-22)

268. Dr. Polich noted there was no visual difference between the marijuana cigarettes and the placebo cigarettes and that this lack of distinction between the two was "one of the biggest assets." (G-22, pg. 5, ¶¶ 7-8)

269. He also noted that the potency was "more than adequate" and that the plant parts in the marijuana used in his research were "well processed material, never seen a seed or a stem, very impressed and pleased with product." (G-21, pg. 6, ¶ ¶ 10-12)

270. Out of 100 research subjects, no more than three complained of harshness according to Dr. Polich. (G-22, pg. 7, ¶ 14)

271. Mr. Strait interview Dr. Billy Martin, a long-time marijuana researcher who also has been involved in the Public Health Service committee that approves or denies protocols for research with NIDA marijuana. (Tr.-892-893, l. 9-22, 1-10) Dr. Martin, however, asked that Mr. Strait submit the standard questionnaire to Aaron Lichtman, Ph.D., because, as Dr. Martin explained, Dr. Martin was more involved in administrative duties while Dr. Lichtman had more familiarity with marijuana on a daily basis. (Tr.-895-896, l. 20-22, 1-9) Dr. Lichtman is an Associate Professor of Pharmacy and Toxicology at Virginia Commonwealth University. (G-28, pg.1)

272. The standard questionnaire was submitted to Dr. Lichtman who completed the answers; he noted that he conducted animal research, not clinical research, with marijuana. (Tr.-896-897, 22, 1-2; G-28, pg. 1)

273. Dr. Lichtman noted that in their studies they receive bulk marijuana from NIDA, and they hand roll their own cigarettes. (G-28, pg. 2, ¶ 1)

274. Although Dr. Lichtman noted that leaves, buds, seed and twigs were contained in the marijuana they received, he did not indicate that his animal studies were adversely impacted. (G-28, pg. 6, ¶ 12, pg. 7, ¶¶ 13, 15)

275. Dr. Lichtman noted that he would prefer a higher potency marijuana than the 3% to 4% potency that they received from the last order in 1999, i.e. 6% to 10%. (G-28, pg. 7, ¶ 13, pg. 9, ¶ 16, pg. 12) And Dr. Lichtman noted that he had not sought a higher potency product. (G-28, pg. 10, ¶ 18)

276. Both Dr. Lichtman and Dr. Martin (during an oral interview by Mr. Strait) mentioned a process of "fortification" whereby if the marijuana's potency is not strong enough, a researcher can infuse the material with more of the active ingredient and thus increase the potency. (Tr.-899, l. 4-10; G-28, pg. 3, ¶ 5)

277. Mr. Strait testified that no one from CMCR indicated that there were some CMCR personnel not willing to be interviewed by Mr. Strait. (Tr.-1071, l. 14-16) Mr. Strait also testified that based upon his check of DEA records, he estimated that there were between 10 and 50 researchers who used or were authorized to use marijuana by DEA. (Tr.-1078, l. 5-21)

278. Mr. Strait did not contact patients who are authorized to use marijuana under the Compassionate Use IND program because they were not researchers. (Tr.-1087, l. 2-18)

279. Mr. Strait testified that a researcher could obtain marijuana from NIDA, could import it or could grow it if the cultivation was limited to the legitimate research purposes. (Tr.-1096, l. 12-22, Tr.-1098, l. 7-11)

See also 21 CFR 1301.13(e)(1)(v). (Dr. ElSohly testified that he was aware that several Schedule I researchers can cultivate marijuana for their own research. Tr.-1500, l. 12-18))

280. Mr. Strait explained that he focused on the CMCR investigators because in May to June 2003, they represented the universe of marijuana researchers that were looking at marijuana's potential therapeutic benefits. (Tr.-1116-1117, l. 21-22, 1-3)

(h) **Testimony of Steven W. Gust, Ph. D.**

281. Steven W. Gust, Ph. D., (Dr. Gust) is a Special Assistant to the Director at the National Institute on Drug Abuse (NIDA) since 1990. (Tr.-1623-1624, 17-22, 1-13) Dr. Gust has a Ph.D. in psychology. (Tr.-1754, l. 1-4)

282. Under the United States Department of Health and Human Services are the Food and Drug Administration (FDA) and the National Institutes of Health (NIH); under the NIH there are 27 separate institutes and centers, and NIDA is one of them. (Tr.-1624-1625, l. 14-22, 1-3; G-34) The PHS [Public Health Service] is the umbrella organization that is over the NIH [National Institutes of Health], and NIDA is one of the institutes that is under the NIH. (Tr.-1688-1689, l. 21-22, 1-14; G-34)

283. NIDA's mission is to support research on causes, consequences, prevention and treatment of drug abuse and addiction. (Tr.-1625, l. 4-7) NIDA also administers the National Drug Supply Program. (Tr.-1625, l. 8-10) In this capacity, NIDA provides controlled substances, Schedules I through V, as well as other substances to researchers. (Tr.-1625, l. 11-21)

284. When a researcher requests marijuana for research from the NIDA Drug Supply Program there are three conditions that have to be met before NIDA distributes the marijuana: (1) There is a peer review for

the scientific merit of the research protocol; (2) The researcher must be a DEA registered researcher; and (3) The researcher needs an approved IND from the FDA. (Tr.-1626, l. 5-19) This latter process is required of all marijuana research requests regardless of funding. (Tr.-1626-1627, l. 20-22,1)

285. The peer review, conducted by a committee formed by the PHS to review protocols, is made up of members from other HHS agencies such as the FDA, NIH and Substance Abuse and Mental Health Services Administration (SAMHSA). (Tr.-1688, l. 16-20; Tr.-1692, l. 1-8) (SAMHSA is the HHS organization that, *inter alia*, promulgates regulations for Narcotic Treatment Programs. 42 CFR § 8.1, et seq.)

286. The PHS peer review committee meets as needed, and the persons on the committee vary according to what expertise is needed, e.g., if the research involves experimenting with a drug to alleviate pain, then a person who has an expertise in pain will be on the committee. (Tr.-1712-1713, l. 13-22, 1-22)

287. The latter requirements are not necessarily unique to marijuana- they apply to any substances requested from NIDA's Drug Supply Program. (Tr.-1627, l. 2-7) However, Dr. Gust noted that the PHS review process was limited to researchers requesting marijuana from NIDA's Drug Supply Program. (Tr.-1646, l. 1-13) If a researcher also wants funding from the NIH, then the researcher's protocol must go through an NIH peer review process. (Tr.-1647, l. 17-22)

288. If a researcher is not looking at the medical application of marijuana, his or her protocol would be subject to an ad hoc review provided through NIDA. (Tr.-1648, l. 1-12) This ad hoc review process generally uses the same guidelines as the NIH peer review criteria in

terms of looking at the scientific significance, the quality of the investigators and the environment. (Tr.-1687, l. 10-22)

289. When asked on cross-examination whether there was a fourth review process, outside of the NIH, conducted by the FDA, Dr. Gust answered as follows. (Tr.-1648, l. 14-19) NIDA only provides peer review for request for materials that are provided by the Government; so if a researcher is working with substances not provided by the Government, then NIH, NIDA and the PHS would not be involved in any review process. (Tr.-1648-1649, l. 20-22, 1-2) Such researchers would just need to file an IND with the FDA and have FDA review their protocol. (Tr.-1650-1651, l. 16-22, 1)

290. During cross-examination, Dr. Gust was asked two times, in essence, if the NIH peer review protocol was superfluous or duplicative of the FDA protocol review. (Tr.-1651, l. 19-22; Tr.-1692, l. 9-14) Dr. Gust responded that the FDA review is primarily for safety uses and not necessarily for scientific merit; so there would be no requirement for a pharmaceutical company to submit to NIH for peer review, i.e., to determine whether their research would be a benefit or not. (Tr.-1652, l. 1-10) Dr. Gust also testified that the May 1999 HHS policy statement (G-24) was not above and beyond what the FDA would require because the policy statement peer review was "just adding one more way of achieving that scientific peer review. It's not above and beyond. It's just an alternative method to achieve that." (Tr.-1692, l. 14-21)

291. Dr. Gust testified that if a research protocol dealing with whole plant marijuana had an approved FDA IND, the researcher would not have a problem obtaining marijuana from NIDA. (Tr.-1717-1718, l. 5-22, 1-21) Dr. Gust also testified that someone who wanted to research smoked marijuana would not necessarily have anymore trouble obtaining NIDA

marijuana than someone who wanted to obtain NIDA marijuana for research with extracts. (Tr.-1719-1720, 4-22, 1-21)

292. Dr. Gust explained that the May 1999 HHS policy statement would likely approve protocols that had specific endpoints as opposed to being indefinitely ongoing. (Tr.-1695-1696, l. 10-22, 1-17; G-24, pg. 3, § IV, 2nd ¶) (See FOF-294-295 for an explanation of the May 1999 HHS policy statement.)

293. "Peer review" is used by NIDA and other HHS subdivisions "where outside expertise is acquired and outside opinions on the scientific merit of specific research proposals." (Tr.-1627, l. 8-17) "Outside expertise" means experts not employed by the Government; peer review panels are set up three times a year for NIH and 90% or more of the reviewers are from the private sector. (Tr.-1627-1628, l. 18-22, 1-7; G-24, pg. 3, § IV, 2nd ¶)

294. Through Dr. Gust, the Government introduced the HHS May 21, 1999 policy statement, which is still extant. (Tr.-1628-1629, l. 8-10, 4-20) This policy statement adopted the criteria that Dr. Gust noted in FOF ¶ 284. (G-24, pg. 4-5) The policy statement detailed the criteria for approval of protocols such as good clinical and laboratory research, a description of an adequate and well-controlled clinical study to evaluate the safety and effectiveness of marijuana and its constituents in the treatment of serious or life threatening therapies, or for a use in which there are no alternative therapies, the extent to which the protocol describes a biopharmaceutical study designed to develop an alternate delivery system 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 constituents on the safety or toxicity of smoked marijuana. (G-24, pg. 2-3)

295. The policy statement also indicated that it was promulgated in order for the United States to comply with Articles 23 and 28 of the Single Convention, which requires the parties (who allow the cultivation of marijuana) to "establish a national agency to control the cultivation and distribution of the crop." (G-24, pg. 1)

296. Prior to 1999, NIH had a standing peer review committee if the researcher wanted Government funding; if the researcher had other funding, NIDA had to put together ad hoc committee from outside experts to conduct peer review. (Tr.-1629-1630, l. 22, 1-13)

297. The pre-1999 standards entailed the following criteria: (1) Will the research advance science? (2) Is the approach valid? (3) Is the protocol innovative? (4) Are the facilities adequate? And (5) what are the qualifications of the researchers? (Tr.-1630-1631, l. 19-22, 1-14) If the research was clinical, then there had to be a showing that the proposals had been reviewed and approved for clinical research. (Tr.-1631-1632, l. 15-22, 1) The latter procedures applied for other controlled substances as well as marijuana since NIDA provides other Schedule I controlled substances for research. (Tr.-1632, l. 3-6; Tr.-1643, l. 15-18) Dr. Gust noted, however, that there are some Schedule I controlled substances that may be obtained from sources other than NIDA for research. (Tr.-1643-1644, l. 19-22, 1-3)

298. The May 1999 HHS policy statement increased interest in research for marijuana; the policy statement was made to increase the standardization of the process. (Tr.-1632-1633, l. 13-22, 1-10; G-24) Through this policy, NIDA added expertise that was not previously available under the pre-1999 standards because NIDA's mission did not include treatment. *Id.* Protocols were now reviewed by a PHS

committee where additional expertise from other NIH and Federal agencies was available. *Id.*

299. The NIH committee, when reviewing protocols, first denies protocols that lack scientific merit. (Tr.-1699, l. 4-14) The rest of the protocols are approved and are scored on a 1 to 5 scale, with one being the highest score. (Tr.-1699-1700, l. 15-22, 1-2) In practice funds are limited so that protocols with the highest scores, 1 or 2, will receive funding before the lower scored protocols. (Tr.-1700, l. 3-17)

300. Dr. Gust noted, however, that it was not difficult to have a protocol approved because the "scientific bar has been set very low, that any project that has scientific merit is approved." (Tr.-18-20)

301. Dr. Gust also explained that if a PHS review committee denies a protocol, the committee will work with the researchers to cure any deficiencies; protocols can be resubmitted. (Tr.-1733-1734, l. 20-22, 1-18; Tr.-1739-1740, l. 17-22, 1-10)

302. Dr. Gust recalled one instance, about ten years ago, when an IND was approved but the NIDA review committee denied the protocol; the researcher did not resubmit the protocol. (Tr.-1738-1739, l. 14-22, 1) In the past ten years, dozens of protocols have been approved by NIDA/PHS. (Tr.-1740, l. 11-21) Dr. Gust later acknowledged that the incident in question happened in 1999 and related to Dr. Ethan Russo; Dr. Russo, who applied for an NIH grant, found alternative funding and so did not resubmit his protocol to the NIH. (Tr.-1745-1746, l. 12-22, 1-22)

303. Dr. Gust testified that in the past ten years there had been non NIH funded researchers who were able to obtain NIDA marijuana; not all of these researchers were part of the CMCR program. (Tr.-1752, l. 16-22) Such grants, however, were not based upon the PHS committee that

reviewed protocols because that committee had not been established yet. (Tr.-1753, l. 1-6) Dr. Gust could not recall if these researchers submitted protocols dealing with the marijuana plant material, but he believed at least half of these studies were clinical studies. (Tr.-1753-1754, l. 7-22, 1-4)

304. Regarding Chemic, whose protocol to obtain marijuana in order to test a vaporizer was recently rejected by the PHS committee, Dr. Gust explained that Chemic could resubmit its protocol. (Tr.-1751-1752, l. 1-22, 1-4) Indeed, the CMCR researchers have been very aggressive about amending their protocols (in the few instances they were denied) to the PHS committee in order to obtain NIDA marijuana to continue their research. *Id.*

305. Dr. Gust testified that the PHS process favored research of marijuana extracts over the smoked marijuana as the ultimate goal. (Tr.-1703-1704, l.12-22, 1-5) But Dr. Gust explained that research with the crude plant material is a necessary first step in demonstrating "proof and principle" before additional research in purifying pharmaceuticals and components, and developing alternative delivery devices could occur. (Tr.-1704-1705, l. 13-22, 1-12)

306. Dr. Gust explained that giving priority to the ultimate goal of developing a marijuana constituent as a medicinal drug over developing the plant material as a medicinal drug is a question for FDA and not for "this program." (Tr.-1705-1706, l. 14-22, 1-8) And the preference to develop an extract over smoking plant material was endorsed by the IOM report, with which NIH and HHS agree with. (Tr.-1706, l. 8-16; R-1, pg. 22, 234) But the bias of ultimately marketing a marijuana constituent as "medicine" over the plant material as "medicine" in and of itself is not a bias at the level of the PHS review. (Tr.-1722, l. 10-20)

307. Another change that resulted from the May 1999 HHS policy statement was that marijuana could now be provided to other research projects outside of NIH as long as those other projects reimbursed NIDA for the cost of the marijuana. (Tr.-1633, l. 11-17; G-24)

308. The May 1999 HHS policy statement applies just for clinical marijuana research; it does not include animal research or research on the deleterious effects of marijuana on humans. (Tr.-1634-1635, l. 12-22, 1-6) The latter studies are not required to go through a PHS committee review procedure. *Id.* However, Dr. Gust also explained that the latter studies would be subject to an NIH or ad hoc system committee review procedure that does not need federal funding. (Tr.-1635, l. 7-15)

309. Dr. Gust's NIDA duties also include oversight of the NIDA contract with the University of Mississippi Research Institute [directed by Dr. ElSohly]. (Tr.-1635, l. 16-19)

310. Dr. Gust, who is familiar with how the NIDA marijuana contract is awarded, explained that he and Dr. Harry Singh develop a statement of work, which outlines the work that needs to be accomplished. (Tr.-1636, l. 5-22) The statement of work is then put into a request for proposal and submitted to the NIDA Contracts Procurement Office, which announces the availability of the contract, receives applications, and conducts the review. (Tr.-1636-1637, l. 22, 1-10)

311. The past contracts have had more than one bidder, and Dr. Gust was aware that for the last contract (March 2005) there were more than two bidders. (Tr.-1642-1643, l. 5-22, 1-14)

312. The proposals are rated by a group of outside experts based upon technical feasibility and costs; the applicant (bidder) with the lowest cost and best technical scores is awarded the contract. (Tr.-1637, l. 10-22)

313. The current contract was awarded in March 2005; this contract was advertised in the Commerce Business Daily, Federal Business Ops. (Tr.-1638, l. 2-17)

314. Dr. Gust found out through DEA that Dr. Craker of the University of Massachusetts had submitted an application to manufacture marijuana, so Dr. Gust sent a notice of competition so that Dr. Craker could submit a bid on the contract (that was awarded in March 2005). (Tr.-1638-1639, l. 18-22, 1-19)

315. Dr. Gust was not aware that NIDA received a formal complaint from a qualified researcher, physician or patient about the quality of NIDA marijuana nor has he ever received any telephone calls concerning such complaints. (Tr.-1639-1640, l. 20-22, 1-9)

(i) **Testimony of Richard Doblin, Ph. D.**

316. Richard Doblin, Ph. D., (Dr. Doblin) obtained a Ph.D. from Harvard University, Kennedy School of Government; his Ph. D. dissertation pertained to the regulation of medical use of Schedule I controlled substances. (Tr.-472-473, l. 6-22, 1-10)

317. Dr. Doblin has no graduate degrees in pharmacology, bio-chemistry or botany; neither does he have a medical degree. (Tr.-709, l. 9-15) Dr. Doblin never worked for HHS; although he applied to work for FDA at one point, FDA did not hire him. (Tr.-709-710, 20-22, 1-22) Dr. Doblin has not worked for a DEA registered pharmaceutical company. (Tr.-711, l. 1-6)

318. In 1986, he founded the Multidisciplinary Association for Psychedelic Studies (MAPS), a non-profit lobbyist organization whose goals include "legalizing" certain Schedule I controlled substances so that such substances are accepted for medical use in treatment. (Tr.-

473-474, l. 11-22, 1; Tr.-477-478, l.1-2, 22, 1-5) Dr. Doblin is the president of MAPS. (Tr.-472, l. 3-5)

319. In 1989-1990, MAPS, i.e., Dr. Doblin, became interested in marijuana as a possible medicine based upon Dr. Doblin's article that claimed that oncologists showed "substantial support" in the medical community for using marijuana to control nausea in patients undergoing chemo therapy treatment. (Tr.-490, l. 9-20)

320. In 1995, Dr. Voth and Richard H. Schwartz, M.D., published *Marijuana as Medicine: Making a Silk Purse out of a Sow's Ear*, Journal of Addictive Diseases, Vol. 14(1), The Hawthorne Press, Inc., 1995. (G-39) This article criticized Dr. Doblin's oncology study by noting that the oncology survey included bench researchers, radiation oncologists and other non medical oncologists who are rarely in a position to make decisions about medications for treatment of chemotherapy induced nausea. (G-39, pg. 17-18) The response was 40% (and not 42% as report in the Doblin article), and in any event was not statistically valid. G-39, pg. 18) Moreover, the Doblin study did not distinguish whether the oncologists surveyed recommended marijuana multiple times on recent occasions or just recommended once ten years ago. *Id.*

321. The authors took their own survey of oncologists in the Summer of 1994. (G-39, pg. 19) About 1,500 surveys were sent, 750 responded and out of those 651 were analyzed; the results were that only 30% believed that marijuana should be rescheduled as a prescription drug, and even if marijuana were reschedule only 32% would prescribe marijuana. *Id.* Of these 30% of responding oncologists that might prescribe marijuana, 74% estimated that they would prescribe fewer than eleven times per year and 16% would prescribe between 11 and 25 times per year. *Id.*

Only 4% estimate that they would prescribe marijuana for their cancer patients 25 times or more a year. *Id.*

322. According to Dr. Doblin, when the synthetic marijuana product, Marinol, became available as a prescription drug, marijuana researchers became "discouraged" and research discontinued. (Tr.-492-493, l. 22, 1-18)

323. Dr. Doblin then contacted Dr. Donald Abrams (who is currently one of the CMCR researchers) to see if Dr. Abrams would be interested in doing marijuana research related to AIDS patients; although he agreed to do so and Dr. Abrams received FDA approval to do so, his protocol was not accepted by NIDA in April 1995. (Tr.-493, l. 19 to 500, l. 4) Dr. Abrams attempts to import the marijuana and to obtain it directly from Dr. ElSohly (and thus circumvent the NIDA process) were, likewise, unsuccessful. (Tr.-502, l. 3 to Tr.-504, l. 19; R-28; R-29)

324. Dr. Doblin sent to Dr. Abrams a facsimile, in which Dr. Doblin discussed suing NIDA because NIDA would not provide the marijuana for Dr. Abrams' research. (Tr.-514, l. 10-21; R-31)

325. However, Dr. Abrams redesigned his protocol, and NIDA agreed to give Dr. Abrams the marijuana he needed for his research and in addition awarded him a one million dollar grant. (Tr.-523, l. 9 to Tr. 525, l. 17)

326. Dr. Doblin also testified that Dr. Ethan Russo had several protocols to research the use of marijuana for migraine headaches rejected back in 1996-1999. (Tr.-527, l. 1 to Tr.-529, l. 11)

327. MAPS also tried to arrange with Chemic, a DEA analytical laboratory registrant, to study a vaporizer as an alternative delivery system to smoking marijuana; this study was to compare how the vaporizer works with various combinations of components and no

clinical research was involved at this point. (Tr.-530, . 4 to Tr.-532, l. 20)

328. Chemic submitted a protocol but its efforts to have the protocol reviewed were not successful. (Tr.-543, l. 7 to Tr.-538, l. 6; R-13; R-14) Chemic and MAPS brought suit in the D.C. Circuit Court of Appeals to have the court compel review of Chemic's protocol. (Tr.-538-539, l. 10-22, 1-21) The suit against NIDA was dismissed. (Tr.-539, 1-21)

329. On July 27, 2005, the PHS review committee, acting for NIDA, sent Chemic a letter; the letter rejected the protocol and gave reasons for the rejection. (Tr.-544, l. 6 to Tr.-549, l. 12; R-52)

330. Dr. Doblin believed that Chemic would not resubmit a revised protocol but would challenge the PHS committee's rejection of the protocol either directly to the committee or in a court. (Tr.-658, l. 18 to Tr.-660, l. 15)

331. Dr. Doblin correctly noted that DEA also required Chemic to submit an application as a DEA researcher before it tested the vaporizer because Chemic's DEA analytical laboratory registration would not cover testing the vaporizer; Chemic's application for research is still pending. (Tr.-662, l. 7-22; Tr.-663, l. 6-10)

332. Dr. Doblin expressed his opinion that based on the letter from NIDA's Nora Volkrow, NIDA was not in business to support "medical" marijuana research and was not authorized by Congress to be in the business of selling marijuana for potential prescription use. (Tr.-551, l. 13-21)

333. Dr. Doblin claimed that the NIDA marijuana has been "low potency" and that an FDA risk-benefit analysis shows that higher marijuana potency means persons will inhale more therapeutic cannabinoids and need to inhale less harmful materials; Dr. Doblin opined that there was a

need to experiment with higher potency strains and with cannabinoids other than THC. (Tr.-552, l. 5-17)

334. Dr. Doblin testified that "NIDA's marijuana, recently in response to our efforts actually, NIDA has claimed that they've got a focus on quality, but in the past, their marijuana would be filled with seeds and sticks and stems and what not * * * It's old, it's harsh and it's stored for years sometimes, and we felt it was an inadequate product." (Tr.-552-553, l. 18-22, 1-12)

335. Dr. Doblin's claim about the past problems with NIDA marijuana containing stems and seeds was based upon an article written by Dr. Ethan Russo and several others concerning the ostensible beneficial effects of cannabis on research subjects. (R-19) One part of this article had two pictures; one picture depicted "loose NIDA cannabis as provided to Compassionate IND patients" and the other picture showed a "close-up" of "debris" from "three NIDA cigarettes." (R-19, pg. 50, Figures 5 and 6). The previous page shows rolled marijuana cigarettes and the canister label, which is dated April 1999. (R-19, pg. 49, Figures 3 and 4)

336. The marijuana cigarettes were distributed by NIDA to physicians who dispensed the cigarettes to patients who qualified for the marijuana under the FDA's program for compassionate or experimental use; the program was eliminated because the demand became overwhelming as the result of the AIDs epidemic. (Tr.-561-562, l. 21-22, 1-16) The patients who initially received marijuana under this program were allowed to continue, and Dr. Russo's article pertained to the marijuana distributed to four of these patients. (Tr.-560, l. 5-20; Tr.-563, l. 11-16)

337. Dr. Doblin testified that he did not know if Dr. ElSohly addressed the complaints in the Dr. Russo's article, and he presumed that Dr.

ElSohly had removed the seeds, stems and sticks from the marijuana. (Tr.-720-721, l. 19-22, 1-14)

338. Dr. Doblin testified about one of the CMCR research patients, Philip Alden, who dropped out of Dr. Israelski's CMCR study based upon Mr. Alden's unsubstantiated claim that the NIDA marijuana caused bronchitis but using marijuana, "legal under California law" helped him. (Tr.-568, l. 22 to Tr.-571, l. 10)

339. Since Philip Alden did not testify, Dr. Doblin testified on his behalf. (Tr.-722, l. 7-22) Mr. Alden complained about NIDA marijuana about four years ago. (Tr.-723, l. 1-7) Dr. Israelski, the CMCR researcher who treated Philip Alden, did not make any complaint about NIDA marijuana on Mr. Alden's behalf. (Tr.-723, l. 8-16) Dr. Doblin did not confirm with Dr. Israelski or any physician who treated Philip Alden as to whether Mr. Alden's claim about the NIDA marijuana was true. (Tr.-725, l. 16-20) Although Dr. Doblin testified that Dr. Israelski advised Mr. Alden to leave the CMCR for health reasons, Dr. Doblin never confirmed this assertion with Dr. Israelski. (Tr.-742, l. 5-13)

340. Although Philip Alden also uses illicit marijuana, he attributed his bronchitis to only using the NIDA marijuana according to Dr. Doblin. (Tr.-723-724, l. 17-22, 1-11; Tr.-724-725, l. 21-22, 1-15) Dr. Doblin could only assume that Mr. Alden used only NIDA marijuana while participating in Dr. Israelski's CMCR study, although Dr. Doblin did not know when Mr. Alden started to use illicit marijuana. (Tr.- 724, l. 12-14; Tr.-725-726, l. 21-22, 1-8) Nor did Mr. Alden inform Dr. Doblin how often or how long he used illicit marijuana. (Tr.-727, l. 4-9)

341. Dr. Doblin testified about an English pharmaceutical company, GW Pharmaceuticals that had developed a pharmaceutical product from plant

marijuana; the product is delivered through a spraying device and is lawfully marketed in Canada. (Tr.-590, l. 8-22)

342. Dr. Doblin testified that the United Kingdom allows GW to grow its own marijuana, hold onto the stocks and develop their own product, which, according to Dr. Doblin, is in compliance with all applicable treaties including the Single Convention. (Tr.-591-592, l. 1-22, 1-11)

343. Dr. Doblin testified that he sought to obtain marijuana from GW, but GW refused because, according to Dr. Doblin, GW was concerned about the perception from FDA and DEA that these agencies would look askance at any product derived from the botanical plant marijuana as opposed to extracts. (Tr.-599, l. 4-15)

344. Dr. Doblin testified that there were no researchers with projects lined up, but he believed there would be if he could obtain an "independent source of supply." (Tr.-583-584, l. 22, 1-22)

345. Dr. Doblin maintained that Dr. Craker's registration was necessary so Dr. Doblin could develop marijuana into an FDA approved prescription medicine, and he needed a DMF for a particular product; when the research commenced the marijuana would be available for potential marketing. (Tr.-603, l. 2-9)

346. Dr. Doblin claimed that an alternative producer would be available so that "we" had the ability to select the strains of marijuana that "we" want to research. (Tr.-603, l. 21-22) Dr. Doblin also claimed that "... we don't have that capability with NIDA's marijuana so that we really need to do a realistic drug development effort, and that requires our own independent source of supply." (Tr.-604, l. 1-4)

347. It was Dr. Doblin's opinion that smoked marijuana or vaporized marijuana in plant form will successfully compete with marijuana extracts. (Tr.-605, l. 9-19) Dr. Doblin also claimed that FDA approval

of such products would be more difficult with NIDA marijuana because NIDA marijuana is "lower potency." (Tr.-607, l. 4-9)

348. Dr. Doblin also complained that NIDA was not authorized to distribute marijuana to companies that wanted to develop a product on a commercial basis. (Tr.-607, l. 10-14) Dr. Doblin speculated that even if "we" had access to NIDA marijuana or from Dr. ElSohly's enterprises, they could charge a monopoly price or even refuse to sell it. (Tr.-607-608, l. 15-22, 1-4)

349. Dr. Doblin testified that he did, indeed, attempt to obtain marijuana on behalf of Dr. Abrams through Dr. ElSohly, but that Dr. ElSohly did not agree to supply Dr. Abrams for "political" reasons. (Tr.-608, l. 12 to Tr.-610, l. 19)

350. Dr. Doblin filed an amicus brief on behalf of Angel Raich in the *Gonzales v. Raich*, 125 S. Ct. 2,195 (2005); Dr. Doblin contended that California's Proposition 215 should not be preempted by Federal law. (Tr.-614-615, l. 19-22, 1-15) Dr. Doblin's position in relation to this case was that marijuana should be available as "medicine" for those who wanted it. (Tr.-632-633, l. 16-22, 1-3)

351. Dr. Doblin also submitted a brief in *United States v. Oakland Cannabis Buyers' Cooperative*, 532 U.S. 483 (2001) on behalf of the appellee/respondent; Dr. Doblin argued that FDA should approve marijuana as medicine pending sufficient data to prove safety and efficacy. (Tr.-619-620, l. 14-22, 1-5)

352. Dr. Doblin addressed the five factor test set forth in *Alliance For Cannabis Therapeutics [ACTS] v. Drug Enforcement Administration*, 15 F.3d 1131, 1135 (D.C. Cir. 1994)[2], which summarized the criteria for

2 (1) The drug's chemistry must be known and reproducible; (2) there must be adequate safety studies; (3) there must be adequate and well-controlled studies proving efficacy; (4) the drug must be accepted by

allowing a substance to become a pharmaceutical drug. (Tr.-620-621, l. 6-22, 1-5) Under the first factor, Dr. Doblin claimed that herbal plant marijuana's drug chemistry is known and reproducible because NIDA has a DMF that the FDA has accepted- so FDA believes that there is a known and reproducible chemistry in the plant. (Tr.-621, l. 6-15) Dr. Doblin later testified that the FDA would not permit marijuana research unless NIDA had a DMF that satisfied FDA that marijuana was consistent and pure enough to do research. (Tr.-652, l. 6-21)

353. Under factor four, Dr. Doblin claimed that the drug must be accepted by qualified experts who accept marijuana as medicine. (Tr.-622, l. 4-6) And under factor 5, Dr. Doblin maintained that the scientific evidence about marijuana is widely available because GW's product, Sativex, has been approved in Canada as medicine. (Tr.-622, l. 6-10; Tr.-642-643, l. 9-22, 1-16)

354. Dr. Doblin maintained that marijuana's chemistry is known and reproducible and can be standardized. (Tr.-629-630, l. 18-22, 1-10) He further opined that one can determine what marijuana's constituents will do because FDA has said that you can assess safety from a plant as a whole and that you do not need to do safety studies on all of the constituents; one just needs to show that the THC content be consistent. (Tr.-1630-1631, l. 11-22, 1-11) He noted that, since FDA issued guidelines for botanical substances, "... it's no longer as uncertain how to develop a botanical product." (Tr.-641, l. 7-12)

355. Dr. Doblin believes that marijuana should be a legal substance for both medical and non medical purposes. (Tr.-633-634, l. 18-22, 1-6; Tr.-639, l. 17-20) Dr. Doblin believed that marijuana should have the same legal status as tobacco, coffee and sugar. (Tr.-639, l. 11-16)

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qualified experts; and (5) the scientific evidence must be widely available.

356. Dr. Doblin admitted to smoking marijuana for recreational use. (Tr.-712, l. 18-19; Tr.-715, l.11) He started abusing marijuana for recreational purposes while he was in college in 1971, and the last time he self-abused marijuana was just last week. (Tr.-718, l. 3-9, 18-21) He self abuses marijuana about once a week or so. (Tr.-719, l. 1-4)

357. Dr. Doblin was asked if the marijuana he used for recreational purposes was "illicit street marijuana" or from marijuana that is in "the stream of HHS-DEA commerce, lawful marijuana?" (Tr.-719-720, l. 18-22, 1) Dr. Doblin answered: "I have never used any marijuana that was from NIDA, nor would I want to. [Laughter.]" (Tr.-720, l. 2-4)

358. Indeed, when Dr. Doblin was asked if marijuana should not be used as patients until FDA has approved it as such, he answered: "... I think the Government should be penalized for blocking medical marijuana research for 30 years." (Tr.-634, l. 7-13) Although Dr. Doblin admitted that it was not ideal to prescribe marijuana due to safety issues, he opined that it was better to leave such decisions to the physician and patient rather than the "police." (Tr.-634-635, l. 14-22, 1-11; Tr.-636-637, l. 22, 1-21)

359. Dr. Doblin agreed that marijuana had abuse potential and that botanical plant products, such as marijuana, are inherently more difficult to bring to market. (Tr.-641-642, l. 20-22, 1-8)

360. Dr. Doblin claimed that MAPS was a pharmaceutical company, albeit without actual facilities; he chronicled his efforts to have other Schedule I controlled substances, such as psilocybin and MDMA, researched to become Schedule I controlled substances. (Tr.-646-647, l. 6-22, 1-4; Tr.-647-648, l. 22, 1-2) Dr. Doblin testified that it was hope to create MAPS own facilities with DEA registrations. (Tr.-647, l. 4-6)

361. Dr. Doblin envisioned his plans for Dr. Craker's registration as follows: "So we hope eventually that Professor Craker would grow for research, and if the research pans out, that the facility would be expanded to provide for prescription use. (Tr.-647, l. 7-10) But Dr. Doblin indicated that he was not looking for a pharmaceutical company to develop a marijuana prescription drug but that MAPS "would do it ourselves. * * * We are acting as a non profit pharmaceutical company, and we would like to be at the other end of the process engaged in actually marketing for prescription use." (Tr.-647-648, l. 21-22, 1-5) And MAPS has no imminent plans to build a production facility to produce Schedule I drugs to be produced and re-scheduled as prescription medication. (Tr.-650, l. 6-15) Dr. Doblin also admitted that MAPS has no pharmaceutical company seeking MAPS' assistance in developing a marijuana prescription medicinal product. (Tr.-702, l. 9-16)

362. Dr. Doblin disagreed with the IOM report that "defined substances such as purified cannabinoid compounds are preferable to plant products..." (Tr.-653, l. 11-22, 1-14; R-1, pg. 22) Dr. Doblin opined that combining THC and cannabidiol in the plant would be a potential anti-anxiety medication. *Id.* Dr. Doblin claimed that the plant form of medication might be less toxic in some ways. (Tr.-654-655, l. 22, 1-5) Dr. Doblin, however, acknowledged that the IOM report tended to favor cannabinoids over the plant material as having more potential for medicine. (Tr.-656, l. 11-15)

363. Although Dr. Doblin testified that his goal was "... trying to get the Public Health Service [PHS] and NIDA out of the picture ..." because they have a monopoly, he also admitted that DEA does not have the

authority to tell NIDA or the PHS to whom these HHS organizations should give marijuana. (Tr.-664, l. 13-21; Tr. 666, l. 2-6)

364. Chemic, the company that has done some research with marijuana to develop a vaporizer device, was supplied with marijuana outside the legitimate channels of DEA regulations through Dr. Doblin (Tr.-668, l. 7 to Tr.-683, l. 8) The chronology of Dr. Doblin's testimony in this regard is as follows.

365. Initially, Dr. Doblin maintained that the marijuana was supplied to Chemic by "DEA-licensed facilities" and that was a chemical analyst that was the only place in the United States that can accept anonymous samples for analysis, the Drug Detection Lab (DDL) in Sacramento. (Tr.-668-669, l. 11-22, 1-4; Tr.-669-670, l. 18-22, 1-9) Then Dr. Doblin admitted: "Well, we had contacted Drug Detection Lab to see if they might be able to send some [marijuana to Chemic]." (Tr.-669, l. 5-13)

366. Then Dr. Doblin admitted that he was the person that contacted a person ("Jeff Zender") at DDL to transfer marijuana to Chemic so Chemic could perform "vaporizer research." (Tr.-671, l. 7-18) Dr. Doblin prevaricated on whether DDL had the authority under DEA law to transfer the marijuana to Chemic under these circumstances. (Tr.-671, l.19 to Tr.-673, l. 9)

367. Then Dr. Doblin stated that marijuana intended for an unknown compassionate use patient was delivered to DDL "for analysis to compare with the marijuana that was coming in from the buyers' clubs." (Tr.-673-674, l. 10-22, 1-2) Although Dr. Doblin denied speaking to any compassionate-use patients directly to transfer their marijuana to DDL, Dr. Doblin indicated that he made it publicly known in having NIDA marijuana evaluated. (Tr.-674, l. 3-16) Dr. Doblin did not try to

obtain the marijuana for this testing directly from NIDA. (Tr.-674-675, l. 17-22, 1-10)

368. Dr. Doblin finally admitted that the compassionate use patients sent marijuana to DDL based on Dr. Doblin's request. (Tr.-675-676, l. 21-22, 1-5) And Dr. Doblin then admitted that it was by his urging that DDL sent the compassionate-use marijuana to Chemic. (Tr.-676, l. 7-10) Dr. Doblin then maintained: "[I]n conversations with Jeff Zender [of DDL]. I understood that DEA came to speak to him about it and that he explained what he had done, and I didn't get the impression that it was necessarily forbidden, but I certainly got the impression that what we wanted to do was to go directly to NIDA, that that would be the preferable approach. ... (Tr.-677, l. 4-11)

369. Dr. Doblin maintained that he thought it would be "legal" for a compassionate use person to send his or her marijuana to a laboratory to verify that what NIDA indicated about the marijuana was true. (Tr.-677-678, l. 13-22, 1-9) Dr. Doblin, however, admitted that, although DDL did the analysis to inform the compassionate use patients what was in the NIDA marijuana, DDL also sent the marijuana to Chemic so Chemic could test the marijuana in the vaporizer. (Tr.-679-680, l. 16-22, 1)

370. Although Dr. Doblin was aware that a DEA -222 order form was necessary to distribute marijuana, he could not say if such a form was used because the compassionate use patients that transferred the marijuana to DDL were anonymous. (Tr.-680-681, l. 5-22, 1-9)

371. Dr. Doblin asked other persons to contact the compassionate use patients to distribute their marijuana to DDL. (Tr.-681 l. 10 to Tr.-683, l. 8)

372. Dr. Doblin will direct Dr. Craker where to send the marijuana if Dr. Craker becomes registered with DEA. (Tr.-721, l. 15-21) Dr. Doblin's plan, assuming Dr. Craker's DEA application is granted, is to work with FDA on a clinical plan, come up with a strategy and then look for researchers who would use marijuana provided by Dr. Craker. (Tr.-740-741, l. 10-22, 1-9)

373. Dr. Doblin explained that MAPS does not subsidize CMCR researchers. (Tr.-733, l. 9-19)

374. Dr. Doblin chronicled the trouble that Dr. Abrams had obtaining permission from NIDA to use the NIDA marijuana for his research. (Tr.-683, l. 22 to Tr.-685, l. 3) However, Dr. Abrams submitted a protocol in 1997, and this protocol was accepted in 1997. (Tr.-683-684, l. 9-21, 1; Tr.-685, l. 4-15) But Dr. Abrams revived his protocol in order to obtain marijuana from the protocol he initially submitted in 1995 or 1996. (Tr.-687, l. 9-22)

375. Dr. Doblin acknowledged that CMCR (for whom Dr. Abrams is one of the researchers) has been able "... to obtain marijuana from NIDA for a number of studies, and that's been very helpful." (Tr.-689, l. 13-18; Tr.-694, l. 14-22, 1-2; Tr.-696, l. 9-22) Dr. Doblin noted that CMCR's goal was not to make marijuana a prescription medicine, "...which is MAPS' explicit goal, so therefore, I think that sends up red flags, and anything that we do gets shut down." (Tr.-689-690, l. 18-22, 1; Tr.-690, l. 12-18) Dr. Doblin testified, however, that CMCR could share its research results with a pharmaceutical company. (Tr.-690, l. 12-18)

376. Dr. Doblin chronicled another person whose protocols to conduct marijuana research were not approved between 1996 and 1999 by NIDA and that person was Dr. Ethan Russo. (Tr.-690, l. 18-22; Tr.-691-692, l. 17-22, 1-14; Tr.-692-693, l. 16-22, 1-4) Since that time period, Dr.

Russo did not pursue anymore research studies with marijuana but joined GW as an advisor on GW's marijuana derived product, Sativex. (Tr.-691, l.1-16; Tr.-693, l. 5-11)

377. Dr. Doblin testified that there was one other researcher who was potentially frustrated that he could not obtain marijuana for NIDA research; this person's name was Paul Consroe. (Tr.-707, l. 1-9) But Dr. Doblin noted that MAPS was unable to persuade Paul Consroe to even submit a protocol. *Id.* Dr. Doblin was not sure if Paul Consroe was a DEA registered researcher. (Tr.-707, l. 10-21) And the events relating to Paul Consroe occurred about ten years ago. (Tr.-708, l. 12-20)

378. Dr. Doblin could not come up with any other names of researchers who were thwarted by NIDA to proceed with marijuana research. (Tr.-709, l. 1-4) And he was aware of just three protocols that had been denied for researchers who sought NIDA marijuana, Dr. Abrams, Dr. Russo and Chemic. (Tr.-704, l. 3-7)

(j) Testimony of Lyle E. Craker, Ph. D.

379. Lyle E. Craker, Ph. D, is a professor at the University of Massachusetts, Department of Plants, Soil and Insect Sciences. (Tr.-12-13, l. 17-22, 1-18; R-3) He has a Ph. D. in agronomy. (Tr.-15, l. 1-4)

380. Dr. Doblin approached Dr. Craker to ask Dr. Craker to cultivate marijuana for research. (Tr..-25, l. 2-8; Tr.-219, l. 5-11) Dr. Craker sought the registration "... to supply a defined marijuana project, find a defined marijuana project to investigators that wanted to do clinical trials with marijuana." (Tr.-33, l.8-16; Tr.-211, l.1-3; Tr.-217, l. 14-20) MAPS would designate the researchers who will obtain marijuana from Dr. Craker, who indicated"... I really have no idea who the potential customers all would be." (Tr.-224-225, l. 22, 1-7) If DEA grants Dr. Craker's application, Dr. Craker will rely on Dr. Doblin to find

customers for Dr. Craker's marijuana. (Tr.-389-390, l.20-22, 1-3) Although Dr. Craker noted on his response to the application questions that he was going to supply marijuana for research using smoked marijuana, at the time of the hearing he indicated that the marijuana would be provided for vaporization studies; although he was concerned about the smoking effects, he did indicate that such studies should not be eliminated entirely. (Tr.-239, l. 21 to Tr.-241, l. 22; R-3)

381. When Dr. Craker wrote a letter, in which he claimed that there was a need for another marijuana supplier for researchers, to Frank Sapienza on June 2, 2003, he had no specific researchers in mind who would have needed an alternate marijuana supply source. (Tr.-256, l. 15 to Tr.-259, l. 3; G-30) Although the Dr. Craker's letter also indicated that a pharmaceutical company would not develop a marijuana drug product without a ready source of supply, Dr. Craker acknowledged that he did not obtain this information from a pharmaceutical company representative. (Tr.-260, l. 2-16; G-30) The letter also indicated that researchers were secretly dissatisfied with the NIDA marijuana, but Dr. Craker testified that he was not personally aware of any specific researcher and that he was not aware of the CMCR research program at the time he wrote the letter. (Tr.-260-261, l. 17-22, 1-13; Tr.-262, l. 5-21; Tr.-263, l. 4-6; Tr.-264, l. 3-6; Tr.-272, l. 10-17; G-30)

382. Dr. Craker had not received any names of researchers from MAPS whom he would supply. (Tr.-226-227, l. 1-22, 1-19) Dr. Craker was not aware of any potency requested by a specific researcher although he heard generally that researchers would want a THC potency range between 7% and 15%. (Tr.-327-238, l. 9-22, 1-8) Dr. Craker was not aware of whether the University of Mississippi (the Research Institute) could produce this THC potency range or not. (Tr.-238, l. 9-14)

383. Dr. Craker has not sent or received any correspondence from any pharmaceutical drug company. (Tr.-228, l. 14-17) And he was not aware of any potential pharmaceutical company customers. (Tr.-235, l. 3-7) Dr. Craker was not aware of any company doing research with the vaporizer and was not aware of what kind of marijuana such a company would need. (Tr.-229, l. 16-22)

384. Dr. Craker's marijuana would be used to develop a marijuana vaporizer, which might eliminate some of the harmful effects from smoking marijuana. (Tr.-35-36, l. 18-22, 1-6) Dr. Craker, in part of his answer to the question of whether the vaporizer would lead to technical advances, stated: "I'm not qualified at this time without something that I can -- a study that's been run by medical doctors under appropriate conditions to judge whether the vaporizer is better than anything else. I don't have that expertise." (Tr.-77-78, l. 17-22, 1-6) Dr. Craker indicated that he himself was not going to work on the vaporizer. (Tr.-230, l. 12-16) Dr. Craker has no current or pending patents relating to growing medicinal plants. (Tr.-238, l. 15-20)

385. When Dr. Craker applied he only had a vague idea that the marijuana produced at the University of Mississippi (the Research Institute) was "relatively low quality." (Tr.-214-215, l. 1-20, 6-10) His information about the quality of the NIDA marijuana came from Dr. Doblin. (Tr.-215-216, l. 11-22, 1-2)

386. Dr. Craker will not grow outdoors but will limit marijuana cultivation to indoor facilities where he can control the environmental factors to grow various strains of marijuana. (Tr.-37, l. 9 to Tr.-39, l. 8) Dr. Craker plans to grow about 25 lbs. of marijuana a year; this estimate was obtained from Dr. Doblin. (Tr.-39-40, l. 20-22, 1-5) Dr. Craker did not know how much table space would be needed to grow this amount

since, he testified, "...I'm not experienced in growing this plant." (Tr.-40, l. 6-12)

387. Dr. Craker testified that he had no past experience growing marijuana or any other controlled substance. (Tr.-79, l. 2-17; Tr.-204, l. 19-22)

388. Dr. Craker maintained that granting his application would further technical advances because "... it would make an advance in the understanding any possible clinical use of marijuana if we were able to supply this to investigators to run trials." (Tr.-17-22, 1) In addition, "... we would learn more about how the environment affects the constituents in the plant material, which would enable, if this does become at some stage down the road here, becomes a useful drug ... they would know the environment it needs to be grown under to produce a clinical marijuana, medical marijuana." (Tr.-76, l. 2-10)

389. Dr. Craker did receive notice that NIDA was taking bids on its 2005 contract to grow marijuana. (Tr.-40-41, l. 22, 1-5; Tr.-249, l. 7-21; Tr.-250-251, l. 15-22, 1) But Dr. Craker did not bid because he believed he had little chance of success after looking at the prospectus; his conclusion was based upon his lack of experience and his lack of desire to analyze illicit marijuana samples. (Tr.-41, l. 6-20; Tr.-277-278, l. 19-22, 1-3) Dr. Craker explained that one reason he did compete to be awarded the contract, was that he did not have the experience that the University of Mississippi (the Research Institute) had. (Tr.-251, l. 2-13)

390. Although Dr. Craker testified that he had the instruments to analyze samples of marijuana (or alleged marijuana), he indicated that: "We could certainly learn the techniques if necessary to do it, the proper procedure." (Tr.-207-208, l. 2-22, 1-2)

391. During cross-examination, Dr. Craker gave the following information about how he would cultivate marijuana. (Tr.-185, l. 11 to Tr.- 205, l. 15) Dr. Craker explained that he would plant the marijuana with standard plant substances such as perlite, vermiculite, peat moss, and common fertilizers such as nitrogen, phosphorous and potassium. (Tr.-185-186, l. 11-22, 1-6) Dr. Craker noted that the " ... commercial media usually is satisfactory for everything we are going to do." (Tr.-186-187, l. 7-22, 1-16)

392. The procedures for planting the marijuana would be based upon the standard methodology for medicinal plants. (Tr.-188, l. 1-9) The marijuana would be initially planted in standard trays and as they germinate they would be moved to larger pots and then to the garden. (Tr.-190-191, l. 8-22, 1-14) The plastic pots in which the marijuana is planted, as well as the nutrients, chemicals and fertilizers are standard although the ratios may vary. (Tr.-192-193, l. 19-22, 1-18) These steps are standard processes used for other plants. (Tr.-192, l. 17-19) Dr. Craker noted that marijuana is similar to other plants in that they all need water and nutrients. (Tr.-205, l. 1-15)

393. Dr. Craker testified that he would have to wait until harvesting and the marijuana has been tested before he could specify the THC level; he would not be able to determine any such specifications from the seedlings. (Tr.-197-198, l. 21-22, 1-12) Dr. Craker explained that if he needed to provide a certain level of THC, the literature indicates that various light regimes could influence THC content. (Tr.-199-200, l. 5-22, 1-6) He also noted that pruning and growing all female plants would have an effect on the THC level but that "... I have not looked into those at depth ..." *Id.*

394. When asked how he would determine THC level at the end of the process, Dr. Craker stated that he would run the appropriate type of laboratory tests but qualified his answer by stating that "...we have not had experience in that ..." (Tr.-200, l. 7-15) Dr. Craker noted that he has standard laboratory equipment such as gas and high pressure chromatographs to measure marijuana THC content. (Tr.-206-207, l. 11-22, 1) But Dr. Craker was unable to say whether he would test for THC content himself or if he would send the marijuana out for testing by a separate laboratory. (Tr.-200-201, l. 19-22, 1-7)

395. Dr. Craker testified that the marijuana would be ready for harvesting as follows: "I assume it would be the maturity, depending on the, the part of the plant that we wanted to harvest. If leaves, you could get almost immediately, but if you want to harvest, if you want to harvest flower buds, you'd have to wait until they appear." (Tr.-195, l. 8-22)

396. After harvesting, the marijuana would be dried in commercially available drying ovens, in which Dr. Craker dries other plant material. (Tr.-196, l. 1-7)

397. Dr. Craker's intent would be to provide plant material to a researcher or pharmaceutical company that would need it for its own research. (Tr.-231, l. 1-7) Dr. Craker would send the plant material in bulk to the researchers, and he did not plan to roll the bulk material into cigarettes. (Tr.-242-243, l. 16-22, 1-6) Dr. Craker indicated that his initial crop would be 25 pounds dry weight of manicured buds, which would not include extracts or any similar derived product from marijuana. (Tr.-236-237, l. 18-22, 1-8; G-3, pg. 2)

398. Dr. Doblin assisted Dr. Craker in preparing the answers provided on the DEA application. (Tr.-351-352, l. 9-22, 1-1-5; G-3) Information about potencies (between 7% and 15%) required by researchers and

alleged complaints from researchers about NIDA marijuana came from Dr. Doblin as well. (Tr.-363, l. 6-16; Tr.-368-369, l. 18-22, 1-9; G-30) In addition, the estimate of the initial marijuana crop at 25 pounds also came from Dr. Doblin. (Tr.-382, l. 19 to Tr.-384, l. 1)

399. Dr. Craker asserted that his application should be granted even if the University of Mississippi's marijuana is of a sufficient quantity and quality. (Tr.-386-387, l. 16-22, 1-8) Under this scenario, Dr. Craker would supply marijuana to any researcher who wanted to do marijuana research but who was not under a Government contract. (Tr.-387-388, l. 14-22, 1-3)

(k) **Testimony of Barbara Roberts**

400. Barbara Roberts past position was working for the Office of National Drug Control Policy (ONDCP) for about 9 ½ years. (Tr.-282-283, l. 16-22, 1-4) She does not have a medical degree, and she was not testifying as an expert. (Tr.-304, l. 2-4; Tr.313, l. 18-19) At ONDCP she was a policy analyst focusing on treatment issues. (Tr.-283, l. 5-16; Tr.-314-315, l. 19-22, 1-22)

401. While Dr. Roberts was still employed at ONDCP, the IOM report pertaining to marijuana was published. (Tr.-293-294, l. 17-22, 1-5; R-1) ONDCP Director Barry McCaffrey's and ONDCP's reaction to the IOM report was "muted." *Id.*; Tr.-327-328, l. 16-22, 1-4)

402. Although Barbara Roberts reviewed the IOM report, she did not issue a written review, and she was not the lead policy analyst who examined the IOM report. (Tr.-331-332, l. 13-22, 1-3)

403. According to Barbara Roberts, ONDCP was skeptical about the feasibility of marijuana being delivered in a non smoked device, but ONDCP believed that research should proceed for marijuana. (Tr.-299, l. 1 to Tr.-302, l. 19)

404. Barbara Roberts maintained that the policy at ONDCP was to oppose marijuana as medicine even after the IOM report was published. (Tr.-339, l. 5-16) But when she was asked on cross-examination if the policy of ONDCP and NIDA was to oppose "medical marijuana," she answered: "No, I said that in terms of the report, that when it came out, that there was no position really taken by the ONDCP, and because they did not take a position, you would not have expected to see NIDA then to come out and take a position on the IOM report." (Tr.-342, l. 7-14) Barbara Roberts did not believe that NIDA would oppose medical research with marijuana. (Tr.-343, l. 2-11)

405. Barbara Roberts took early retirement from ONDCP and filed an Equal Employment Opportunity complaint against ONDCP; the complaint is pending. (Tr.-334-335, l. 16-22, 1) She professed that she held no grudge against ONDCP as a result of filing the complaint. (Tr.-336, l. 10-21)

(l) Testimony of John Vasconcellos

406. John Vasconcellos was a California state legislator until November 2004 when he retired. (Tr.-393-394, l. 11-22, 1-14) As a legislator he sought successfully to pass a bill to make marijuana a medicine in California, only to have the bill vetoed by the Governor. (Tr.-394-395, l. 21-22, 1-12)

407. After Proposition 215 passed by referendum in California, Mr. Vasconcellos introduced legislation to create a university based research center for cannabis, which resulted in the creation of CMCR. (Tr.-395, l. 13 to Tr.-398, l. 7) Fifteen research proposals were funded over a five year period. (Tr.-398-399, l. 18-22, 1-5) All fifteen proposals approved at the state level were approved by NIDA. (Tr.-418, l. 1-9) NIDA provided marijuana for this research. (Tr.-399, l. 17-19) A few of these

fifteen studies were discontinued before they were completed because they could not solicit enough research subjects (patients) initially. (Tr.-419-420, l. 3-22, 1-4)

408. Although the current research will continue, there are no additional funds in the foreseeable future because of California's budget crisis. (Tr.-400-401, l. 6-22, 1-21) It is possible that funding for CMCR will be renewed, but the California budget is still "in the red" by several billion dollars. (Tr.-401-402, l. 22, 1-9; Tr.-405, l. 3-17)

(m) **Testimony of Dale Gieringer, Ph. D.**

409. Dale Gieringer, Ph. D., (Dr. Gieringer) has a Ph. D. in engineering economic systems. (Tr.-492, l. 1-16; Tr.-423, l. 17-19) He works on economics and policy analysis, and his focus in these regards pertains to FDA drug regulation. (Tr.-423-424, l. 20-22, 1-12)

410. He has been very active in lobbying for passage of "medical marijuana" laws, has been active in the National Organization for the Reform of Marijuana Laws (NORML), and helped promote California's Proposition 215. (Tr.-425-426, l. 3-22, 1-1-2; Tr.-426 l. 13 to Tr.-428, l. 16) He has been a consultant on behalf of the "legalization" petitioners in recent Supreme Court cases, such as *Gonzales v. Raich*. (Tr.-446-447, l. 20-22, 1-20)

411. He also is on the National Advisory Council (NAC) for CMCR; the NAC oversees CMCR to ensure CMCR adheres to its legislative mandates. (Tr.-428, l. 5 to Tr.-431, l.3; Tr.-431-432, l. 20-22, 1-3)

412. Dr. Gieringer testified that CMCR's goal was "pure" research, but CMCR did not have as its mission developing a marijuana medicinal product through working with a pharmaceutical company. (Tr.-433-434, l. 21-22, 1-15) A pharmaceutical company, however, could cite the CMCR studies in an NDA, but such a pharmaceutical company would

have to create its own Drug Master File (DMF). (Tr.-435-436, l. 12-22, 1-11; Tr.-439-440, l. 11-22, 1)

413. Dr. Gieringer believed that a pharmaceutical company could not use NIDA marijuana because it would have to start a whole new manufacturing process with a new DMF. (Tr.-436-437, l. 22, 1-20) Dr. Gieringer also believed that it would not be possible for a drug pharmaceutical company to have access to NIDA's DMF because it is confidential. (Tr.-438-439, l. 17-22, 1-10)

414. On cross-examination, Dr. Gieringer acknowledged that a pharmaceutical company could obtain the raw material from NIDA. (Tr.-451, l. 11-19) Dr. Gieringer, however, was still skeptical that such an arrangement could be made because if NIDA or the Research Institute changed any aspect of the marijuana, the DMF would have to be updated and because, from an economic perspective, a pharmaceutical company would have less control over the price or amount if it purchased it from NIDA. (Tr.-449, l. 16-20; Tr.-451, l. 3-10) Dr. Gieringer acknowledged that, although he was aware of DMFs, he had not been in the pharmaceutical industry himself. (Tr.-464, l. 6-16)

415. Dr. Gieringer also noted that when CMCR's uses its current funding of 9 million dollars, no additional funds have been allocated by the State of California at this time. (Tr.-441, l. 1-22) He noted, however, that CMCR is looking into obtaining money from private sources, such as private pharmaceutical companies. (Tr.-445-446, l. 22, 1-10)

416. Dr. Gieringer confirmed that CMCR researchers were able to obtain NIDA marijuana for their research. (Tr.-444, l. 4-15)

(n) **Congressional testimony of Nora D. Volkrow**

417. Nora D. Volkrow, M.D., the Director of the National Institute on Drug Abuse (NIDA), National Institutes of Health (NIH), U.S. Department of Health and Human Services, gave a statement to Congress concerning the abuse and potential for medicinal use of marijuana. (R-31)

418. Dr. Volkrow noted that marijuana was the most commonly used illicit drug, more than 95 million Americans, age 12 and older, tried marijuana at least once according to a 2002 survey, and among the 1.5 million adult substance abuse treatment admissions (age 18 or older), 154,000 were admitted as primary marijuana abusers. (R-31, pg. 1) She noted an American Medical Association study, which found that early exposure to marijuana is associated with a lifetime of subsequent drug problems. (R-31, pg. 2, ¶ 4) She concluded the testimony by noting that marijuana is not a benign drug and that it is illegal and has significant adverse health and social consequences associated with its use. (R-31, pg. 4, ¶ 3) She noted that using smoked marijuana as "medicine" is problematic due to its adverse health consequences. *Id.*

419. Dr. Volkrow highlighted the many deleterious health consequences of using marijuana, which included the possibility of addiction, disrupting short-term memory, attention and judgment, impairment of coordination and balance, increasing heart rate, and overall dissatisfaction with mental and physical health for those who were lifetime abusers. R_31, pg. 2) She even noted some developmental problems with children of women who smoked marijuana while pregnant. (R-31, pg. 2, ¶ 5)

420. Marijuana withdrawal symptoms, which can last several days to a week, include increased anxiety, increased drug craving, sleep difficulties and decreased appetite. *Id.*

421. New research shows that marijuana can affect almost every organ in the body, from the central nervous system to the cardiovascular, endocrine, respiratory/pulmonary and immune systems. *Id.* Marijuana in smoked form can impact the respiratory and increase the likelihood of some cancers. *Id.*

422. Dr. Volkrow, however, noted the potential for medical uses that marijuana had, and she cited the IOM report in this regard. (R-1; R-31, pg. 2-3) She also highlighted the clinical studies that were being conducted into the potential for medical use, including 17 CMCR studies, which had been approved for research with marijuana by HHS. (R-31, pg. 3, ¶ 6)

(o) **Other documentary sources concerning the abuse of marijuana**

423. A January 2003 report from NIDA (*Report on the Rare Disease Activities a the National Institutes of Health*) found that marijuana is the most commonly used illicit drug in the U.S., with recent estimates from SAMHSA of 14.6 million users in the past month and particularly heavy use in adolescent populations, e.g. over 20% of all high school seniors. (G-43, pg. 9, 3rd full ¶) Of the 3.5 million people who met criteria for past-year cannabis abuse or dependence in 2001, more than 2/3 were between the ages of 12 and 25 years. *Id.* An estimated 852,000 persons 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 about half of these individuals were age 25 or younger. *Id.*

424. The NIDA report also found that sufficient research has been conducted to confirm that the use of cannabis can produce serious physical and psychological consequences. (G-43, pg. 9, 4th full ¶) The use of a large amount in a short period of time may induce hallucinations, delirium and other symptoms consistent with a psychotic episode. *Id.* Chronic users 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. *Id.*

425. In July 1995, Jon Gettman petitioned DEA to reschedule certain controlled substances, including marijuana, from Schedule I to Schedule III. *Drug Enforcement Administration; Notice of Denial of Petition*; 66 Fed. Reg. 20,038 (2001) (Hereinafter cited as the "Petition.") (G-44) DEA denied the petition after receiving extensive information from HHS that marijuana does have a high potential for abuse and should remain in Schedule I. (G-44, pg. 20,038) In denying the Petition, DEA cited from the Congressional record the following in regard to marijuana: "[T]he consequences of illegal use of Schedule I drugs are well documented, particularly with regard to physical health, highway safety, and criminal activity." (G-44, pg. 20,039, column 1)

426. In denying the petition, the DEA Administrator explained: "Physical dependence and toxicity are not the only factors that are considered in determining a substance's abuse potential. The actual use and frequency of use of a substance, especially when that use may result in harmful consequences such as failure to fulfill major obligations at work or school, physical risk-taking, or even substance-related legal problems, are indicative of a substance's abuse potential." (G-44, pg. 20,040, 3rd column) The Administrator also found: "There is evidence that

individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or to the community." *Id.*

427. The Administrator also found: "The magnitude of the demand for marijuana is, however, evidenced by the Drug Enforcement Administration (DEA) / Office of National Drug Control Policy (ONDCP) statistics. 2Data on marijuana seizures can often highlight trends in the overall trafficking patterns. The DEA's Federal-Wide Drug Seizure System (FDSS) provides information on total federal drug seizures. FDSS reports total federal seizures of 699 metric tons of marijuana in fiscal year 1997, 825 metric tons in fiscal year 1998 and 1,175 metric tons in fiscal year 1999. (G-44, pg. 20,041, column 1)

428. The Administrator also found: "Individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such substances. The 1998 NHSDA suggests that 6.8 million individuals use marijuana on a weekly basis (SAMHSA, 1998), confirming that marijuana has reinforcing properties for many individuals. The FDA has not approved a new drug application for marijuana, although research under several INDs is currently active. Based on the large number of individuals who use marijuana, it can be concluded that the majority of individuals using cannabis do so on their own initiative, not on the basis of medical advice from a practitioner licensed to administer the drug in the course of professional practice." (G-44, pg. 20,041, column 1-2)

429. The Administrator noted that illicit drug use involved about 14.8 million Americans or 6.7% of the population on a monthly basis. (G-44, pg. 20,047, 2nd column) "The most frequently used drug was marijuana, with 11.2 million Americans (5.1% of the U.S. population) using it

monthly." *Id.*; G-44, pg. 20,050, 1st column; pg. 20,051, 2nd column) Among the substances abused by teenagers, marijuana is the most widely used illicit drug. (G-44, pg. 20,047, 3rd column, last ¶)

430. NIDA published the *National Drug Threat Assessment 2005* in February 2005. (G-45) The report found that although marijuana use by teenagers and college students peaked in the 1990s, demand is still higher for this drug than for any other illicit drug. (G-45, pg. 1, 2nd ¶; pg. 8, last ¶) And the report noted that despite recent declines, "the prevalence of marijuana use among these age groups was still considerably higher in 2003 than in 1991, before rates of use began to rise." (G-45, pg. 10, last ¶)

431. Perceptions by adults as well as adolescents who perceive marijuana as harmful have generally decreased since 1991, and these perceptions parallel the increase in marijuana use in older teens and young adults. (G-45, pg. 11, last full ¶) The NIDA report cited data that indicated that "marijuana-related treatment admissions, too, have increased markedly over time- from 5.9 percent of all drug-related admissions in 1992 to 15.1 percent in 2002." (G-45, pg. 13, 2nd ¶)

432. The NIDA report concluded that "[t]he market for marijuana is strong and stable throughout the United States and should remain so given the drug's wide appeal to users..." (G-45, pg. 25, 2nd full ¶)

433. The NIDA report states that "[t] prevalence of marijuana and the continuing high demand for the drug underlie its stability as one of the foremost drug threats. More than 95% of state and local law enforcement agencies describe the availability of the most widely abused illicit drug as high or moderate, and 75% of illicit drug users aged 12 or older report current use of marijuana." (G-45, pg. 2, 1st full ¶) The report noted that "[d]omestic marijuana production appears to be

increasing ..." (G-45, pg. 1, 4th ¶) Amount of available illicit marijuana is also increasing as noted in an increase of estimates from 2001 to 2002. (G-45, pg. 6, 1st full ¶)

434. The NIDA report found that "... in reality marijuana is not harmless. Marijuana's effects can include those problems attendant to cigarette smoking as well as problems with distorted perception and loss of coordination, which can contribute to household, occupational, or vehicular accidents." (G-45, pg. 3, 1st full ¶)

435. THC potency levels of illicit marijuana have increased from about 3% in 1994 to 9% in 2002. (G-45, pg. 7, last full ¶)

436. *Who becomes cannabis dependent soon after the onset of Use? Epidemiological Evidence from the United States: 2000-2002*, Chen, Chuan-Yu, et al., Drug and Alcohol Dependence 79 (2005), pg. 11-22, is an article publishing the results of a study of the risk of becoming cannabis dependent within 24 months after the first use of cannabis. (G-49, pg. 12, under "Abstract") This article noted that marijuana is "one of the most commonly consumed illegal drugs worldwide and has become a public health concern in recent decades. (G-49, pg. 12, 1st sentence under "Introduction") The study found that from the sample that 3.9% of first time users developed a cannabis syndrome within 24 months of the first-time use. (G-49, pg. 12, under "Abstract")

437. In *The Church of the Living Tree; Denial of Application*, 68 Fed. Reg. 17,403 (2003) and *Marion "Molly" Fry, M.D; Revocation of Registration*, 67 Fed. Reg. 78,015 (2002), the DEA Deputy Administrator denied an application to manufacture marijuana and revoked a physician's DEA registration based upon her unlawfully distributing marijuana under the guise of her medical practice, respectively. The Deputy Administrator explained in both final orders

the dangers of using marijuana, i.e. "... numerous significant short-term side effects and long term risks linked to smoking marijuana, including damage to brain cells; lung problems such as bronchitis and emphysema; a weakening of the antibacterial defenses in the lungs; the lowering of blood pressure; trouble with thinking and concentration; fatigue; sleeplessness and the impairment of motor skills." 68 Fed. Reg. at 17,405 and 67 Fed. Reg. at 78,017.

438. A United Nations' World Drug Report 2004 provided the following information. (G-64) Of the estimated world population that abuses drugs (185 million or about 3%), by far the most widely abuse drug is marijuana. (G-64, pg. 1, ¶ 1) Cannabis has been abused at least once in a year by over 150 million people. *Id.*

(p) **The Center for Medicinal Cannabis Research (CMCR) Act**

439. The Center for Medicinal Cannabis Research (CMCR) was a California statutory enactment to create a research program for the medical use of marijuana at the University of California. (G-32; Cal Health & Safety Code § 11362.9) Clinical research was authorized for AIDS, cancer, glaucoma, seizures or muscle spasms associated with chronic, debilitating condition, or other serious illnesses if resources are available and medical information justifies the research. (G-32; § 11362.9(a)(5).

440. When CMCR research proposals are evaluated , "... the program shall use a peer review process that is modeled on the process used by the National Institutes of Health, and that guard against funding research that is biased in favor of or against particular outcomes." (G-32; § 11362.9(c)) When awarding grants, CMCR is directed to model "...programs administered by the National Institutes of Health,

including peer review evaluation of the scientific merit of applications." (G-32; § 11362.9(e)(2))

441. "The [CMCR research] program shall consult with the Research Advisory Panel [,] analogous agencies in other states, and appropriate federal agencies in an attempt to avoid duplicative research and the wasting of research dollars." (G-32; § 11362.9(g))

442. A February 22, 2001 news article concerning the initial CMCR studies noted "[f]our proposals out of 13 submitted from various California research institutions were recommended for funding by the CMCR's independent Scientific Review Board following rigorous scientific review, with full approval pending final review by state and federal regulatory agencies." (R-33) The article then noted that these protocols would be forwarded to FDA, NIDA and DEA for final approval. *Id.*

(q) **Sativex**

443. GW Pharmaceuticals (GW) published in the *Therapeutics Products Directorate*, published by Health Canada; this publication announced that GW's product, Sativex® had been approved as a pharmaceutical drug product in Canada. (G-52) The product is described as a cannabis based medicine derived from the marijuana extracts THC and cannabidiol. (G-52, pg. 1) It is indicated for treatment of neuropathic pain in multiple sclerosis for adults and is ingested into the mouth through a spray device. *Id.*

444. On October 4, 2004, Americans for Safe Access (ASA) filed a "Request for Correction of Information Disseminated by HHS Regarding the Medical Use of Marijuana" with HHS. (G-53A) ASA, and advocacy group that represents the interests of "medical marijuana patients" sought corrections of conclusions made about marijuana by

HHS as cited in *Drug Enforcement Administration; Notice of Denial of Petition*; 66 Fed. Reg. 20,038 (2001) ("Petition"), *supra*. (G-53A, pg. 6-9) ASA filed this petition under the authority of the Data Quality Act, 44 U.S.C. § 3502(1), which according to the ASA petition allows them to submit proposed corrections to any errors made by a Federal agency.

445. The ASA petition maintained that HHS should correct the Petition by noting that studies establish the efficacy of marijuana in the treatment of several diseases, that there is substantial consensus among experts that marijuana is effective in treating some diseases, that the chemistry of marijuana is known and reproducible, and that marijuana has a currently accepted use in treatment in the United States. (G-53A, pg. 2) The petition in its bibliography references cited two articles by Dr. ElSohly; one was a chapter in a book and the other was an article Dr. ElSohly co-authored with two others. (G-53A, pg. 11, 12)

446. On April 12, 2005, GW wrote a letter to HHS in response to the ASA petition. (G-53) After describing the product (consistent with the description published in *Therapeutics Products Directorate*, Health Canada (G-52)), the GW letter notes that the ASA petition cited three articles, which discussed Sativex®. (G-53, pg. 1, 2)

447. GW's response letter asserted: "The data do not support the contention that herbal cannabis ... is safe and effective for treating the medical conditions that were examined in these trials." (G-53, pg. 2) The letter then explained that herbal cannabis is not a homogenous substance unlike Sativex® which contains THC and cannabidiol in a near ratio of 1 to 1. *Id.* The letter explained that herbal cannabis generally contains very little cannabidiol and that herbal cannabis will vary greatly in its composition depending on the circumstances of it cultivation. (G-53, pg. 2-3)

448. GW's letter explained that herbal cannabis is only the starting point for deriving any potential medicinal products and that herbal cannabis is analogous to raw opium, which is only the raw product base for developing various pharmaceutical products. (G-53, pg. 2) GW's letter also expressed skepticism that herbal cannabis could be delivered in a dosage form that is consistent in composition in an identifiable and reliable amount of medication. *Id.*

449. Dr. Craker's counsel asserted at the hearing on December 16, 2005, that HHS had not responded to the ASA petition. (Tr.-1838-1839, l. 21-22, 1-3) There is no response from HHS to the ASA petition in the record.

(r) **Documentary evidence related to the Single Convention Treaty**

450. In a letter, dated March 4, 2003, by then-Chief of DEA's Drug & Chemical Evaluation Section Frank Sapienza to Dr. Craker, Mr. Sapienza explained that DEA "continues to have international treaty and legal concerns regarding your application." (R-29, pg. 1, 3rd ¶) This letter provided no further details about treaty issues.

451. In a letter, dated July 1, 2002, to U.S. Congressman John W. Olver, the then-DEA Administrator, Asa Hutchinson, explained his position on the additional registration of another manufacturer of marijuana as it applied under the Single Convention. (R-55) The letter explained: "The Single Convention requires that 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." (R-55, pg. 1)

452. Then-Administrator Hutchinson's letter continued to explain: "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." *Id.*

453. This letter further explained: "The United States has long been the leader among nations committed to international drug control. Our country has recognized since the early 1900s that cooperative efforts among nations in combating drug abuse are critical to protect the health and general welfare of the American people as well as citizens of all nations. Furthermore, the examples set by the United States in the area of drug control have often set the patterns followed by other nations. The United States must therefore demonstrate a continuing commitment to the Single Convention and other drug control treaties." (G-55, pg. 1-2)

454. The Research Institute of the University of Mississippi and DEA entered into a Memorandum of Agreement (MOA), dated October 7, 1999 (by the last signatory). (G-78, pg. 1, 9) The MOA permitted the Research Institute to extract THC for a pharmaceutical company to develop the product into a medicinal suppository. (G-78, pg. 2) (A third bulk manufacturing registration application filed by the Research Institute to actually launch this extract product is pending. (R-79))

455. The MOA noted, in relation to the Single Convention, the following: "In accordance with articles 23 and 28 of the Single Convention ... private trade in "cannabis" is strictly prohibited. [footnote omitted] Therefore, the Center [Research Institute] shall not distribute any

quantity of marijuana to any person other than an authorized DEA employee." (G-78, pg. 2)

456. The MOA explained DEA's position on the Single Convention as follows: "The Single Convention does not prohibit private trade in 'cannabis preparations,' however. A 'cannabis preparation,' within the meaning of the Single Convention, is a mixture, solid or liquid containing cannabis, cannabis resin, or extracts or tinctures of cannabis. The THC that the Center will extract from marijuana would be considered such a 'cannabis preparation.' Therefore, the Center may, in accordance with the Single Convention, distribute the crude THC extract to private entities ... ." G-78, pg. 2-3)

457. The HHS "Guidance on Procedure for the Provisions of Marijuana for Medical Research" set forth the following regarding the Single Convention:

> "The United States is also a party to the Single Convention on Narcotic Drugs, an international narcotics control treaty. Parties to the Single Convention have agreed to limit production, distribution, and possession of cannabis and cannabis resins to authorized medical and scientific purposes (Art. 4). In addition to these and other controls, Articles 23 and 28 of the Single Convention provide 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. 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." (G-24, pg. 1, § I, 3rd ¶)

458. During the hearing, Dr. Craker tendered a document entitled "United Kingdom National Cannabis Agency: Protocol." (R-26) Initially, the ALJ did not admit this exhibit because there was not indication who issued the exhibit, how it came to be issued and whether the exhibit was an official document. (Tr.-594-595, 598)

459. The ALJ admitted this exhibit (over Government objection) when Dr. Craker presented e-mails from AD MacFarlane, Chief Inspector, Drugs Branch, Home Office. (G-26, Exhibits A-C) Exhibit C indicated that the document in issue was in final form and had been effective since April 2005. Exhibit B, however, indicated that the document was "an internal working document" and had "not been published."

460. This document from the Home Office, Drugs Branch, indicated in the pertinent part that whenever a producer harvests cannabis for use solely as the raw material for the production of cannabis-based pharmaceuticals or research, the cannabis "will be deemed to have taken place between the 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;" (G-26, pg. 2, ¶ 6. b))

II. CONCLUSIONS OF LAW AND ARGUMENT

A. Analysis under 21 U.S.C. §§ 823(a)(1)-(6)

Under 21 U.S.C. § 823(a), "[T]he Attorney General shall register an applicant to manufacture controlled substance in schedules in Schedule I … if he determines that such registration is consistent with the public interest and with United States obligations under international treaties … ." Since the Attorney General must make an affirmative finding that the registration is consistent with the public interest and applicable treaties, Dr. Craker bears the burden of proof. Title 21 C.F.R. § 1301.44(a) explicitly states that such applicants "shall have the burden of proving that the requirements of such registration pursuant to … 21 U.S.C. [§] 823(a) are satisfied."

All factors set forth in 21 U.S.C. § 823(a) need not be present for the

Deputy Administrator to deny an application for a DEA Certificate of Registration. Rather, the Deputy Administrator may rely on any one or a combination of these factors, giving each the weight he deems appropriate, in determining whether a registration should be revoked. See, Richard J. Lanham, M.D., 57 Fed. Reg. 40,475 (DEA 1992); Henry J. Schwartz, Jr., M.D., 54 Fed. Reg. 16,422 (DEA 1989); Neveille H. Williams, D.D.S., 51 Fed. Reg. 17,556 (DEA 1986).

i. Factor 1

Under this factor, Dr. Craker has the burden of proof to demonstrate the following: maintenance of effective controls against diversion of particular controlled substances ... in schedule I ... 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. 21 U.S.C. § 823(a)(1).

a. Need for a second marijuana manufacturer because the current supplier's marijuana allegedly is of insufficient quality and potency

1. Alleged stems and sticks in the marijuana cigarettes

Dr. Craker's claims that another marijuana bulk supplier is needed because the NIDA marijuana produced by the Research Institute is of inferior quality (i.e., has sticks and stems) and is of insufficient potency for use in clinical researchers. In support of these contentions, Dr. Craker offered dubious and dated material.

One of the first exhibits presented to DEA was a letter, dated March 11, 2003, from Ethan Russo, M.D. (Dr. Russo) to DEA's then Chief of the Chemical and Drug Unit, Frank Sapienza. (G-30B) Dr. Russo's first "criticism" was: "I have never said that NIDA is incapable of producing a quality product, but merely that their efforts do not result in material that is representative of domestic, Canadian or European clinical cannabis." (G-30B, pg. 1, 5th ¶)

First, Respondent never presented any evidence of what is representative of marijuana in Canada or Europe, much less any evidence of how Dr. Craker would produce marijuana that would represent Canadian and European "clinical" marijuana. Nor is there any validity to the complaint that NIDA marijuana should represent domestic "clinical" marijuana. (Dr. Abrams made a similar comment in his trip report comments by indicating that the NIDA marijuana should mimic what is found in the San Francisco area. (G-21, pg.7, ¶ 13)

Dr. ElSohly explained that he never received a formal complaint about this issue, and the comment made no sense because the variety of illicit marijuana varies considerably depending on what part of the country the marijuana came from. (FOF-197) Moreover, Dr. El Sohly explained that clinical research that employs blind investigations must ensure uniformity in the marijuana, and such a goal would be severely curtailed by mimicking marijuana cultivated in different parts of the country. *Id.*

Dr. ElSohly's conclusions are unassailable because they not only are logical

but also because Dr. ElSohly has been qualified as and testified as an expert in, *inter alia*, the cultivation, research and potency of marijuana. And even if this issue of mimicking illicit marijuana were a real issue, Respondent, through Dr. Craker or from any other source has not offered any evidence whatsoever to indicate how he would address this "problem."

Dr. Russo' letter also made another unsubstantiated claim: "NIDA continues to supply seeded material that is poorly cured, and relatively impotent." (R-30B, pg. 1, 5th ¶) As "proof" of this claim, Respondent offered into evidence an article by Dr. Russo, which purported to show pictures of seeds and stems from a NIDA marijuana cigarette. (R-19, pg. 50, Figure 6) These depictions, however, were from an RTI canister of marijuana cigarettes manufactured in April 1999. (R-19, pg. 49, Figure 4)

Dr. ElSohly credibly testified, when shown the picture from the Russo article, that the stems and seeds were too large to roll into a marijuana cigarette without puncturing the rolling paper. (FOF-192-194) He also credibly testified that the pictures of the stems and seeds appeared much larger in the picture than their actual size and that the pictures appeared to be from raw material rather than the cigarettes. (FOF-194)

Respondent offered a statement in rebuttal from Al Byrne, a co-author of the article and "a long-term cohort of five federally supplied cannabis patients." (R-57, ¶ 4) Commenting on the Figure 6 picture, Al Byrne's statement noted the

picture and accompanying descriptions "accurately depicts the marijuana leaves, seeds and stems, and the sizes of the leaves, stems and seeds **relative to each other**, as they existed at the time the marijuana cigarette was unrolled and the photographs were taken in my presence." (Emphasis supplied.) (R-57, ¶ 8) The statement, however, never explains whether Figure 6 is enlarged or not. Indeed, just by comparing the picture of the "Loose NIDA Cannabis as Provided to Compassionate IND Patients" in Figure 5 to the "Close-up of Debris from Three NIDA Cannabis Cigarettes" in Figure 6, it is readily apparent that Figure 6 is an enlargement. (R-19, pg. 50)

What makes Respondent's evidence even more suspect in this regard is that both Dr. ElSohly and RTI's Ken Davis (through his affidavit) noted that much earlier in the NIDA program, the Research Institute deseeded the marijuana to the point where the marijuana was too fine. (FOF-190, 224) Dr. ElSohly testified that the Research Institute worked with a company in Canada to design a special deseeding machine to remove all stems, seeds and heavy particles so that RTI no longer has to accomplish this function. (FOF-191) Ken Davis in his affidavit completely corroborated Dr. ElSohly's testimony in this regard and, significantly, noted that "RTI has not received any recent complaints about seeds or stems in their finished product." (FOF-224)

Moreover, more recent and credible evidence refutes Respondent's contention that the NIDA marijuana has too many sticks and stems. The CMCR

researchers, who were interviewed by DEA commencing in September 2003, either did not have any complaints about the marijuana in this regard or actually complimented the marijuana. Dr. Granted noted he visited the Research Institute at the University of Mississippi and noted that the marijuana was mostly devoid of seeds and stems. (FOF-241) Dr. Polich commented that the marijuana was well processed, that he never saw a seed or stem and that he was very impressed and pleased with the product. (FOF-269)

Even if one assumes there was a problem with the stem and seeds in the current marijuana (rather than basing such a claim on a dubious photograph of marijuana produced in 1999), Dr. Craker offered not one shred of testimony of what he would do about this "problem." Moreover, Dr. Voth, testifying as a qualified expert on marijuana, explained that he had never seen any sources that indicated that seeds and stems caused a greater irritation in the marijuana except for "street rumors." (FOF-103)

2. Alleged "harshness" of the NIDA marijuana

Dr. Craker, besides the March 11, 2003 Russo letter, sent Frank Sapienza a copy of a January 24, 2003 news article from the San Mateo County Times in support of his contention that an alternative marijuana supplier was needed because of the lack of quality of the Research Institute marijuana. (FOF-252) Although the article, referring to the CMCR studies, is entitled "Doctors want better marijuana for study," the article never identifies, much less quotes, any

CMCR researcher who made such a complaint. (G-30A)

When Dr. Israelski was presented with this article, he noted that he never made such comments, that the article misrepresented his views and that he was so concerned about the article that he stopped reading this paper and contemplated writing to the editor. (FOF-253) This article is completely inaccurate given the overall information that DEA received from the CMCR researchers about the NIDA marijuana and given Dr. Israelski's comments. (FOF-233-270)

This news article quoted a CMRC research subject, Phillip Alden, who allegedly said he dropped out of the study because of the "low quality of the pot," which supposedly caused him to contract bronchitis. (G-30A, ¶ 5) Phillip Alden never testified to try and substantiate his claims, but Dr. Doblin testified on his behalf. (FOF-338-340) Mr. Alden's complaint was four years ago, and Dr. Doblin never conferred with Dr. Israelski or any other physician as to whether there was any validity to Mr. Alden's bronchitis complaint. (FOF-339) Mr. Alden's claim that he had to leave the CMCR study for health reasons likewise was never substantiated with Dr. Israelski. *Id.*

Dr. Israelski explained that a patient's perception of the quality us often times different than the researcher's perception. (FOF-254) Had there been any reports from the CMCR researchers that numerous patients left the CMCR studies because of the "low quality" of the marijuana, there still would be a question of whether the marijuana was of sufficient quality or not judged from the researchers'

point of view. In any event, Mr. Alden is very much the exception and not the rule as to patients dropping out of the studies due to the "low quality" of the NIDA marijuana. (FOF-233-270)

Several CMCR researchers mentioned a few patient complaints about the "harshness" of the marijuana, but in context these comments were inconsequential. Dr. Grant, who was head of CMCR, commented that "occasionally" a patient complained of "harshness" that produced a cough. (FOF-242) He noted that Dr. Wallace had not experienced any such complaints, and Dr. Wallace confirmed this fact. (FOF-242, 257)

Although Dr. Ellis noted that some patients complained the marijuana smoke was harsh, Dr. Ellis explained that most, if not all, of his subjects were experienced marijuana users and, even more significantly, only one patient dropped out of the study because of "harshness." (FOF-245) Dr. Ellis also commented that the "harshness" issue did not adversely impact his research. *Id.* Dr. Cory-Bloom noted that one out of ten patients complained about the harshness, but she could not tell if the complaints related to a placebo as opposed to an actual marijuana cigarette. (FOF-248) Dr. Israelski noted that he never recalled any patient complaining about the freshness of the marijuana. (FOF-251)

Dr. Abrams answered "no" when asked if any patients expressed complaints about the marijuana's "freshness." (FOF-262) Dr. Abrams explained that even good or smooth marijuana" may feel harsh to users and cause a cough. *Id.* Dr.

Abrams further noted that only a few patients dropped out of his studies due to "harshness," i.e. a total of four out of fifty dropped out due to "harshness." (FOF-266) Dr. Polich did note that three patients complained that the marijuana was "harsh," but that was just three patients out of a hundred." (FOF-270)

Dr. ElSohly credibly testified that he never received any formal complaints about the marijuana's "harshness," that there was no way to tell if the placebo or the marijuana was causing the harshness, that the patients who complained about "harshness" were limited and that no research had been curtailed due to this "harshness" issue. (FOF-183-185, 187-189) Dr. ElSohly noted that some humidity would be lost from marijuana that had been stored a long time, but such an issue had nothing to do with the quality of the marijuana. (FOF-186) But the affidavit from RTI's Ken Davis, and corroborated by Dr. ElSohly's testimony, explained that even this problem was alleviated by RTI providing instructions on how to humidify the marijuana. (FOF-163, 223) Significantly, Ken Davis indicated that RTI had not received any complaints about the marijuana since before some time in July 2002. *Id.*

Dr. Voth credibly testified as an expert that with all of marijuana's constituents, smoking marijuana can be harsh on the throat and lungs. (FOF-87) Moreover, such harshness effects are not necessarily related to the potency of the marijuana but are the result of the fact that marijuana is smoked. (FOF-102)

3. Alleged lack of potency

Although Dr. Grant noted that there had been some difficulty obtaining marijuana potency from 6% to 8%, he also noted that the range of potency provided by NIDA was acceptable. (FOF-236-238) Dr. Grant also noted that an 8% potency was perhaps the highest potency range that the studies could use. (FOF-239) Dr. Ellis noted that a request for 8% potency really tested at about 7% potency. (FOF-244, 246) Dr. Ellis, however, commented that NIDA was "very responsive" to this issue and that "potency has not been a limiting consideration" in his research. *Id.*

Dr. Abrams noted that the potency was not consistent based upon a potency variation between 3.9% requested and 3.5% received. (FOF-260) Dr. Abrams noted that it was NIDA that informed CMCR that the potency for this particular study had been downgraded. *Id.* Thus, this issue was not a problem with the Research Institute marijuana per se but with the NIDA requirements. Although Dr. Abrams mentioned the disparity between a requested shipment of 8% and the actual potency of 7.4%, Dr. Abrams commented that the Research Institute was "very responsive" to this disparity. (FOF-182)

Both Drs. Wallace and Polich explicitly noted that they were satisfied with the potency provided by NIDA. (FOF-256, 269)

Dr. ElSohly credibly testified that the Research Institute could produce bulk marijuana with a potency of up to 15%, has produced bulk marijuana outdoors of

14% potency and on a larger scale (50 to 100 kilograms) is capable of cultivating outdoor marijuana from 10% to 13% potency. (FOF-136, 149) The institute also produces *sensimilla* (seedless) marijuana and has the capability of producing potencies for this type of marijuana between 15% and 24%. (FOF-160)

Dr. ElSohly addressed the remarks made by several of the CMCR researchers that one batch of marijuana was ordered at 8% potency but came tested at less than 8%. (FOF-177-182) There was never a formal complaint although a CMCR representative made the comment about the discrepancy during a phone call to Dr. ElSohly; CMRC never requested that the batch be re-sent. (FOF-177) Dr. ElSohly also credibly testified that marijuana is never produced at an exact amount but within a standard, 20% plus or minus the exact potency sought. (FOF-178) The Research Institute's range was 10%. (FOF-179) The batch in question actually tested at 7.4%, which was well within the higher standard, plus or minus 10% range set by the institute. (FOF-178-179) Thus, the variance was never significant enough for CMCR to "scratch" the initial batch and send another batch. (FOF-180)

Furthermore, Dr. ElSohly found out that when CMCR actually gave the 7.5% potency marijuana to the subjects, they could not tolerate that high a potency; the research resumed when the Research Institute sent a 6% batch in place of the 7.4% batch. (FOF-181)

b. Need for a second marijuana manufacturer based upon interpretation of 21 C.F.R. § 1301.33(b)

Although Respondent has not come close with its burden-of-proof obligation to demonstrate an actual need for a second cultivator of marijuana, Respondent maintains that Dr. Craker's application should be granted simply because the applicable statutes and regulations require such an outcome, particularly based on Respondent's interpretation of 21 C.F.R. § 1301.33(b). This simplistic argument should be rejected because it does not comport with the actual language of 21 C.F.R. § 1301.33(b).

Respondent argues, under 21 C.F.R. § 1301.33(b), that DEA must register another marijuana cultivator, i.e. DEA must register additional manufacturers even though the existing number "is capable of producing an adequate and uninterrupted supply." Respondent's interpretation that this regulation **requires** this result is incorrect; the regulation states that the "Administrator shall not be required to limit the number of manufacturers ... to a number less than consistent with maintenance of effective controls against diversion ... ."

The phrase "shall not be required" denotes discretion. In other words, the phrase means the Administrator "does not have to." This phrase by no means can be interpreted to mean that the Administrator must or has no choice but to register additional manufacturers. Not only is Respondent's interpretation wrong based upon the clear wording of the regulation, Respondent's interpretation would require DEA to add additional manufacturers no matter what other factors under

Section 823(a) would call for the denial of the application. In essence, Respondent's interpretation of Regulation 1301.33(b) would simply require the additional registration of manufacturers no matter what the circumstances as long as there would be "maintenance of effective controls against diversion" under Section 1301.33(b)

However, "[i]t is well established that the Deputy Administrator is not required to make findings with respect to each of the above-listed factors [21 U.S.C. § 823(a)(1)-(6)], but has discretion to give each factor the weight he deems appropriate, depending upon the facts and circumstances in each case." This principle was announced in *Johnson Matthey, Inc.; Approval of Registration*, 60 Fed. Reg. 26,050, 26,052 (1995), in which DEA granted an application for a bulk manufacturer registration of methylphenidate over the objections of a current manufacturer.

c. There is no competition issue because Respondent is seeking a contingent DEA registration while Respondent seeks to find a pharmaceutical company able and willing to develop a medicinal marijuana plant product

1. DEA's long-standing policy against shelf registrations

On September 18, 1975, DEA published a policy statement, *Registration of Importers; Statement of Policy and Interpretation*, 40 Fed. Reg. 43,745 (1975), in which it was announced that DEA would no longer grant import registrations for Schedule I and II controlled substances on a contingent basis, i.e. only in case such imports are needed on an emergency basis. The Acting Administrator noted that

such "contingency reserve" registrations are "unnecessary and also, administratively burdensome." 40 Fed. Reg. at 43,746.

This "long-standing policy" was applied in the denial of an application for List I chemical manufacturer's registration; the applicant just needed the registration for a one-time transaction. *Performance Construction; Denial of Application*, 67 Fed. Reg. 9,993 (2002). This policy was also applied in *Manufacture of Controlled Substances: Notice of Registration*, 69 Fed. Reg. 8,696 (2004). One of the objectors to Houba, Inc.'s, application to manufacture oxycodone and hydrocodone, argued that Houba would not use the registrations if the applications were granted. The final order found that there was enough evidence in the record to indicate that Houba would utilize the registrations and that if Houba did not use them, Houba would retire the registrations. 69 Fed. Reg. at 8,697.

2. Respondent's lack of proof that Dr. Craker's registration would result in a pharmaceutical company developing a marijuana plant drug product

Dr. Martin, an expert in pharmaceutical drug development, testified on behalf of Dr. Craker that it would be unlikely that a pharmaceutical company would seek to develop a marijuana pharmaceutical drug product without a consistent source of supply. (FOF-9-10, 19-21) Based upon this testimony, Respondent seeks an inference that once Dr. Craker is registered, pharmaceutical companies will materialize to develop a marijuana drug product because they'll be assured that Dr. Craker will supply them with a consistent source of supply. Such

an inference on its face is highly speculative, to say the least, and it is amply refuted by the record.

First, even if one considers Dr. Martin's testimony without looking at all the other factors that make it extremely unlikely that any pharmaceutical company will "jump on the band wagon" to develop a marijuana plant pharmaceutical drug, the reality is that there is not one pharmaceutical company "waiting in the wings." Although Dr. Doblin claimed MAPS was a pharmaceutical company, he also testified that it was his hope that MAPS would own its own facilities and have its own DEA registration one day. (FOF-360) Dr. Doblin testified that MAPS was not looking for a pharmaceutical sponsor but would "do it ourselves." (FOF-361)

Dr. Doblin's plans are highly speculative; there is no telling if MAPS will ever become an actual pharmaceutical company. Until and unless there is a pharmaceutical company actually seeking an alternative source of supply to develop marijuana plant as a pharmaceutical drug, any registration granted to Dr. Craker will be a shelf-life or contingent registration.

But the record is chock full of facts that makes Dr. Doblin's dream of a pharmaceutical company developing a plant marijuana medicinal product even less of a probability. Although it was Dr. Doblin's personal belief that extracts or purified cannabinoid compounds would not necessarily be more preferable to the plant material for development of a pharmaceutical drug, the IOM report, which as Dr. Gust testified is endorsed by the NIH and HHS, clearly had a contrary

conclusion. (FOF-306, 362) This fact makes it less likely that any pharmaceutical company will seek Dr. Craker's marijuana plant material.

What makes Respondent's premise even more improbable are the inherent problems with developing a botanical product as opposed to developing a synthetic product. Although this issue was not highlighted during Dr. Martin's testimony, it was discussed at some detail by Dr. Auslander and Dr. Voth. (Although both Dr. Martin and Dr. Auslander were qualified as experts in new drug development, Dr. Auslander, unlike Dr. Martin, did have some experience with botanicals. (FOF-10, 27, 35, 36))

Dr. Auslander credibly testified that synthetic drugs have an established purity and can be more readily quantified and qualified over time while botanicals are much more complex because they have a variety of constituents are not easily identified and require greater effort and resources to establish. (FOF-38) With a botanical it is much harder to maintain purity and consistency than it would be for a synthetic drug. (FOF-40) Although FDA will allow "markers" to be used to identify components in the early stages of drug development, FDA in the later stages would require the chemical constituents characterized and quantified or at the very least the "markers" would have to be well established. (FOF-39, 44)

Dr. Auslander noted that these problems are compounded if the botanical has components of varying pharmacological materials. (FOF-39) The more constituents a botanical has, the more difficult it is to evaluate the botanical; with

100 or more constituents, more interactions take place, the chemistry is more complex, and the engineering that is required to isolate, quantify, establish and understand the botanical is that much more complex. (FOF-42) A large number of constituents presents exponential, as opposed to linear, permutations. *Id.*

Dr. Auslander's testimony in this regard is re-enforced by the testimony of Dr. Voth who was qualified as a medical expert in internal medicine and as an expert in marijuana as it pertains to its effects, abuse on humans and its constituents. (FOF-84) Dr. Voth testified that about 480 substances have been identified in the marijuana plant and of these substances 66 have been identified as cannabinoids. (FOF-85) He also credibly testified that all 66 cannabinoids have not been studied so it is difficult to determine whether all are active. (FOF-86) He explained that there is a sense that some cannabinoids are more active than others; for example Delta 9 THC, Delta 8 THC and cannabidiol are cannabinoids that have been identified as being active. *Id.* But all the cannabinoids have relative degrees of activity. *Id.* Dr. Voth explained that the other 420 or so constituents contain tars and turpines and there is a concern of what happens when these substances enter a persons' lungs because these constituents probably have a similar physiological effect to tobacco. (FOF-87)

Three other hurdles for a drug pharmaceutical company would be the costs of developing a new drug product, which Dr. Martin estimated to be $800,000,000 less opportunity cost, the additional regulatory requirements of dealing with a

controlled substance (as opposed to a legend drug), the reluctance of physicians to use controlled substances (again as opposed to legend drugs) and competitive products already on the market. (FOF-24-26)

Another hurdle is that a pharmaceutical company would have to develop its own Drug Master File (DMF). Both Dr. ElSohly and Dr. Gieringer testified to such. (FOF-167, 169, 412-413) Given all the problems that Dr. Auslander testified about for botanicals, developing such a DMF would not be an easy task. (FOF-47-49)

Under these circumstances, it is almost inconceivable that any pharmaceutical company is waiting in the wings for Dr. Craker to start cultivating marijuana so that a marijuana plant drug product can be developed. It is even more speculative that MAPS will ever develop any infrastructure to develop this type of a product. The conclusion is clear; Dr. Craker's registration in regard to developing a marijuana plant drug product is contingent.

Moreover, there is no reason that a pharmaceutical company could not attempt to obtain marijuana through NIDA for research. (FOF-124) Although it was Dr. Doblin's belief that NIDA would not allow a pharmaceutical company to have NIDA marijuana for research, there is nothing in the contracts to support such an assertion. (FOF-332; G-12, pg. 2, § B. 1; G-13, pg. 2, § B. 1) Indeed, Dr. Gust noted that if any researcher who wanted to work with whole plant marijuana had an approved FDA IND, the researcher would not have a problem obtaining NIDA

marijuana. (FOF-291) Dr. Gust never qualified this testimony with the fact that the researcher could not be a part of a pharmaceutical company.

d. "Competition" as that term is used under 21 U.S.C. § 823(a)(1) is afforded by a competitive bidding process

Competition is afforded through a bidding process. NIDA publishes a notice to accept bids for its marijuana contract in the Federal Register. (FOF-124) The bids are not disclosed to the public or the other bidders. *Id.* (As of November 1999, bids were accepted every five years, instead of three years as was the case prior to 1999. (FOF-130)) Dr. Gust testified that others beside the Research Institute bid on past contract announcements. (FOF-311)

Dr. Gust sent the Federal Register announcement to Dr. Craker, and Dr. Craker acknowledged that he received it. (FOF-314, 389) Dr. Craker admitted that he did not submit a bid to compete for the NIDA contract because he did have the experience, and he did not want to test samples as required by the contract. (F)F-389) Dr. ElSohly explained that the sample-testing requirement could be out-sourced under the NIDA contract. (FOF-153-153)

Although Respondent seeks to define "competition" by merely allowing other cultivators to manufacture marijuana, the DEA's current system is a reasonable (and perhaps the only) interpretation of "competition" under Section 823(a)(1) as it applies to marijuana. There are three reasons why the bidding system is justifiable as "competition" under the circumstances.

First, the marijuana bidding system can easily be distinguished from the

Schedule II bulk system. In the latter situation, DEA will assess the "competition" issue by allowing as many manufacturers or importers to be registered as necessary to supply the market as long as by registering the additional importer or manufacturer, "there would be no increased difficulty in controlling diversion ..." *Noramco of Delaware v. Drug Enforcement Administration*, 375 F. 3d 1,148, 1,153 (D.C. Cir. 2004); *Johnson Matthey, Inc.; Approval of Registration*, 60 Fed. Reg. 26,050, 26,052 (1995). Not only is there a great commercial demand for such products, the companies seeking such registrations are established importers or manufacturers of Schedule II controlled substances. Thus, under these circumstances, the number of the Schedule II registrants is limited; the industry is an oligopoly. Marijuana, on the other hand, has an extremely limited demand as a Schedule I controlled substance, and under these circumstances, it would make no sense to treat it like a Schedule II commercial drug.

e. The bidding system is a reasonable method to afford competition under Section 823(a)(1) because, *inter alia,* marijuana is the most commonly abused drug

1. Extent of marijuana abuse and health consequences

Marijuana is unique to all other controlled substances in the amount and extent of its abuse. Dr. Craker seeks a DEA registration to manufacture and distribute the most abused form of marijuana, the plant material, which is ingested by smoking or inhaling through a "bong." (FOF-72, 95) Marijuana is the most commonly available and abused drug in the United States. (FOF-95, 418, 427-428, 430, 432-433) It is, indeed, one of the most widely abused drugs by

teenagers. (FOF-429) Marijuana abuse is particularly alarming as a drug of abuse for younger persons who are more likely to become dependent or long-term abusers the earlier in age that they start using marijuana. (FOF-96, 418, 423, 428, 430, 432-433) There are severe deleterious health consequences related to marijuana (FOF-419, 421, 424, 434, 437) as well as tremendous negative social consequences. (76, 426, 436) Marijuana is the most widely abused drug in the world. (FOF-438)

2. Evidence from Dr. Grinspoon to "rebut" testimony of Dr. Voth

Respondent offered into evidence a chapter from the book, James Bakalar and Lester Grinspoon, M.D., Marihuana, the Forbidden Medicine, 137-154 (Yale University Press, 1993) (G-21) The ostensible reason for admitting this book excerpt was to rebut Dr. Voth's testimony about the deleterious consequences of marijuana abuse. (Tr.-2056, l. 13-22) The Government tendered, and the ALJ admitted, the preface to this book, pages ix through xiii. (G-96)[3]

First, Dr. Grinspoon's book excerpt would not only have to refute Dr. Voth's testimony on the harm caused by marijuana, but the book excerpt would have to rebut all the other (and much more credible) evidence of the harm caused by marijuana. Nora D. Volkrow, M.D., Director of NIDA, gave testimony before Congress, and such testimony included the many serious social and health ramifications resulting from marijuana abuse. (FOF-417-421) Two other studies

3 This exhibit was admitted post-hearing. See ALJ memorandums of January 24, 2006, and February 2,

from NIDA, one published in 2003 and the other in 2005, corroborate Dr. Volkrow's Congressional testimony in the assessment of marijuana's harm (FOF-423-424, 430, 434) In the *Drug Enforcement Administration; Notice of Denial of Petition*; 66 Fed. Reg. 20,038 (2001), the DEA Administrator, in denying a petition by Jon Gettman to reschedule marijuana, chronicled the severe health consequences resulting from marijuana abuse. (FOF-425-426) In other DEA final orders, DEA has reiterated the severe health consequences of marijuana abuse. (FOF-437) *The Church of the Living Tree; Denial of Application*, 68 Fed. Reg. 17,403 (2003); *Marion "Molly" Fry, M.D; Revocation of Registration*, 67 Fed. Reg. 78,015 (2002). It should also be noted that these sources post-date Marihuana, the Forbidden Medicine, which was published back in 1993.

In the preface to Marihuana, the Forbidden Medicine, Dr. Grinspoon reveals his extreme bias early on by noting: "I had become convinced that cannabis was considerably less harmful than tobacco and alcohol, the most commonly used legal drugs." (G-96, pg. ix, 1st ¶, xii, 1st full ¶) Dr. Grinspoon also evinces a bias in his preface by claiming marijuana has medical benefits, even though the notes "... most of the evidence on marihuana's medical properties is anecdotal." (G-96, pg. xii) In contrast, Dr. Voth, although noting his opposition to using plant marijuana for recreational purposes, voiced support for research of marijuana's components leading to medical use. (FOF-113, 115-116) Dr. Voth

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even published an article, which suggested guidelines for how to use "medical" marijuana in the states that had passed "marijuana medical" acts. (FOF-114)

Another critical distinction, is that Dr. Voth testified and was cross-examined. Dr. Grinspoon never testified. This factor weighs heavily in Dr. Voth's favor.

3. Evidence from Dr. Grinspoon to "rebut" an article of Dr. Voth

During the hearing, through the testimony of Dr. Voth, the Government introduced into evidence an article co-authored by Dr. Voth, *Medical Marijuana: A survey of Teenagers and their Parents*, Clinical Pediatrics, April/May 2001. (G-40) The article, based upon a sample survey taken of teenagers and their parents in Ohio and Virginia, which concluded that 28% of the parent group versus 55% of the teen group believed that passage of state referenda on medical marijuana would make it easier for teens to smoke marijuana for recreational purposes. (FOF-72)

Respondent sought to admit an affidavit of Rodney Skager, Ph. D., and a bar graph accompanying his affidavit. (R-58) The affidavit and bar graph describe a California survey, as compared to an eastern and regional survey, which showed that in 1997-1998, the national and regional abuse of marijuana by teenagers increased while for the same period the California abuse by teenagers leveled off or slightly declined. *Id.* Respondent tendered this exhibit as rebuttal to Government Exhibit 40 because it would rebut the inference that state "medical marijuana" acts would not lead to an increase in marijuana use.. (Tr.-2053-2055;

"Motion to Admit Additional Evidence in Rebuttal," January 5, 2006, pg. 1-2)

The Skager affidavit and graph does not rebut Dr. Voth's article because the two articles surveyed entirely different regions of the country. (G-40; G-58) Moreover, Dr. Skager's bar graph shows a significant and steady increase of marijuana abuse for teenagers in the national and northeast sample. (G-58) And the California rate of marijuana abuse is still above what the national rate is and almost comparable to the northeast abuse rate. *Id.*

The Government introduced "Marijuana Use and the Response to Proposition 215 among California Youth, a Special Study from the 1997-98 California Student Survey" (hereinafter "CSS 1997-98"), because it was the report that pertained to the subject matter of Dr. Skager's affidavit and was the report that Dr. Skager, *inter alia*, wrote for and submitted to the California Department of Alcohol and Drug Programs. (G-94) The CSS 1997-98 report indicates: "Marijuana was the illicit drug used most frequently by students in grades 9 and 11, and the second most popular in grade 7 after inhalants." (G-94, pg. 1, ¶ 4) Although Dr. Skager's affidavit and CSS 1997-98 indicated that marijuana abuse by high school students stabilized since 1995, the CSS 1997-1998 report indicates: "However, six-month rates in California have stabilized at very high levels ..." (G-94, pg. 1, ¶¶ 4-5) This statement would negate the conclusion that California students perceive Proposition 215 as not having an impact on additional marijuana abuse.

The CSS 1997-1998 report noted: "Students overestimated the percentage of

their classmates who have used marijuana, particularly those who used at least once a month." (G-94, pg. 4, ¶ 3, under "Perceived Peer Use") This conclusion would negate to some degree the conclusion that high school students do not perceive an increase in marijuana use as a result of the passage of Proposition 215.

CSS 1997-98 also concluded: "Large majorities of students at all grade levels rated frequent use (daily or almost daily) as harmful. However, since 1990 the harmfulness rating for frequent marijuana use has gone down in California as use has increased." (G-94, pg. 5, ¶ 2 under "*Perceived Harm and Availability*") The report also discusses marijuana use and perception among "Continuation School Students." (G-94, pg.8, ¶ 1) As explained in the report: "Continuation schools are a type of alternative education program focused on preventing youth from failing school and dropping out. * * * Continuation versus comprehensive high schools forms a natural demarcation of youth who are at relatively high or low risk for substance abuse. Previous research has indicated that students use drugs at a much higher rate at continuation than at regular high schools (Austin, 1992)." (G-95, pg. 65, ¶¶ 2-3)

Amongst the conclusions reached about Continuation Students in relations to marijuana were: "In comparison to same-age regular public school students, continuation school students use marijuana earlier and more heavily. * * * Fewer continuation school students thought that frequent use of marijuana was 'extremely harmful.' Finally, more continuation than regular students held positive views about Proposition 215, specifically as the initiative pertains to non-medicinal use and

prospects for future use." (G-94, pg. 8, ¶ 1) These conclusions about this high-risk group of students specifically rebut the general conclusion that students did not perceive a pro-abuse message based upon Proposition 215.

The "7th Biennial Statewide Survey of Drug and Alcohol Use among California Students in Grades 7, 9, and 11" is a follow-up study to the CSS 1997-98 report by Dr. Skager and Gregory Austin. (G-95) It is published by the California Attorney General's Office in the Summer of 2001, but its finding relate to the Winter 1997-1998. (G-95, pg. 1)

This report found: "Also of concern is the softening of perceived harm from frequent marijuana use in all grades." (G-95, pg. 10, ¶ 2; G-95, pg. 13, ¶ 5) The report also notes that 64% of 9th graders and 77% of 11th graders perceive marijuana as easy or fairly easy to obtain. (G-95, pg. 10, ¶ 3) And 43% of 9th graders and 49% of 11th graders believed that 50% or more of their classmates used marijuana at least once a month. (G-95, pg. 10, ¶ 4)

When the latter findings and conclusions of these reports are taking in context, there is ample reason for concern about marijuana abuse especially among young people. (G-94; G-95) And when these reports are placed in the context of the many other reports and evidence concerning the abuse marijuana, they are only look at a fraction of the problem. Ultimately, the "rebuttal" of Dr. Voth's article (G-40) by the affidavit of Dr. Skager (R-58) makes very little difference in the "big picture" even if one believes that Dr. Skager's affidavit is true rebuttal evidence.

f. Competition under Section 823(a)(1) and the Single Convention

Third, under the Single Convention on Narcotic Drugs (1967), *18 U.S.T. 1407,* T.I.A.S. No. 6298, New York, March 30, 1961, ratified by the United States, 1967, Articles 23 and 28, the United States is obligated to maintain one national cannabis agency to oversee the cultivation and distribution of all cannabis cultivated within the United States for medical and scientific purposes. The competitive bid system is much more consistent with the Single Convention than allowing multiple cannabis registrants spread out all over the country. Moreover, this interpretation also would be in accord with the HHS policy and policy statement, which implements the Articles 23 and 28 in this manner. (G-24)

Under Section 823(a)(1), Dr. Craker has the burden of proof to demonstrate that his registration would be consistent with the six factors under Section 823(a)(1)-(6) **and** the Single Convention. In *United States v. LaFroscia*, 354 F. Supp. 1338, 1341 (S.D. N.Y. 1973), the District Court rejected a challenge to an indictment charging the defendant with unlawful importation of marijuana. The District Court reached its conclusion based not only on its interpretation of the Controlled Substances Act but also based upon its construction of the Single Convention as a separate and alternative ground to deny the defendant's challenge. See also, *United States v. Rodriquez-Camacho*, 468 F. 2d 1220, 1222 (9th Cir. 1972), which held that 21 U.S.C. § 841(a)(1) is a permissible method by which Congress may effectuate the American obligation under the Single Convention,

and 21 U.S.C. § 801(7), which states: "The United States is a party to the Single Convention ...designed to establish effective control over international and domestic traffic in controlled substances."

So the issue under the treaty is whether registering Dr. Craker as a second and separate marijuana cultivator would be permissible under the treaty. The answer is a "no." Articles 23 and 28 require the parties to establish a government agency to oversee the cultivation of marijuana[4] Specifically, the parties must designate the areas where marijuana can be cultivated, license such cultivators, and through the government agency purchase and take possession of all marijuana crops as soon as possible. Article 23, § 2(a)-(d). Thereafter, the Government entity shall have the "exclusive right of importing, exporting, wholesale trading and maintaining stocks ..." Article 23, § 2(e).

Based upon the wording of Article 23 and the Commentaries, pg. 278, ¶ 2 and pg. 283, the Single Convention contemplates multiple private cultivators of opium or cannabis who sell their crops to a government agency as soon as the harvest is complete (or at least no later than four months from the end of the harvest). The Government then has a monopoly on the sales of the opium or marijuana. Article 23, § 2(e).

As further background to this issue, it should be noted that opium is not even allowed to be cultivated anywhere in the United States based upon DEA's

4 Although Article 23 refers to opium, Article 28 mandates that Article 23 should apply to cannabis. See

long-standing policy. *Statement of Policy and withdrawal of Proposed Regulations*, 42 Fed. Reg. 28,560 (1976); *Chattem Chemicals, Inc., Grant of Registration to Import Schedule II Substances*, 71 Fed. Reg. 9.834, 9,835 (2006). All opium must all be imported from designated countries as set forth in 21 C.F.R. § 1312.13(f). 71 Fed. Reg. at 9,836. In this context, DEA's (and HHS's) policy of compliance with the Single Convention by having one supplier bid on a contract every five years is a reasonable interpretation of the Single Convention and a reasonable accommodation of the Single Convention with the existing laws and Government agencies that regulate the manufacture and cultivation of marijuana.

In *Malm v. Immigration and Naturalization Service (INS)*, 16 Fed. Appx. 197; 2001 U.S. App. LEXIS 18178 (4th Cir. 2001), a native of Togo overstayed her visa while visiting the United States. INS sought deportation (removal) proceedings against her, and she belatedly requested an asylum hearing under the Convention Against Torture (CAT). The INS denied her request for CAT asylum because her motion to reopen the proceedings was after the time period allowed by INS regulation. She appealed and argued that CAT overruled any procedural provisions of the INS. The reviewing court held that INS was entitled to follow its procedures and that such a "choice represents a reasonable accommodation of conflicting policies that were committed to the agency's care by the statute, [the reviewing court should not disturb it unless it appears from the statute or its

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Commentary on the Single Convention (Commentary), pg. 313, ¶ 6.

legislative history that the accommodation is not one that Congress would have sanctioned. *Chevron*, 467 at 844 ..." *Id.* at 202-203.

In the present case, DEA's and HHS's policy represents a reasonable interpretation and accommodation of the Single Convention given the existing Government structure and especially in light of Respondent's alternative interpretation. While the Single Convention calls for designations where the marijuana will grow, DEA, by requiring the Research Institute to have a secure registered location, complies with the Single Convention in this manner. 21 U.S.C. § 822; 21 C.F.R. §§ 1301.71(a) and 1301.72(a). While the Single Convention requires the marijuana (or opium) cultivators to deliver their crops to a Government agency, having the one supplier who works through NIDA is a reasonable accommodation to the treaty. (FOF-151) And while the Single Convention requires that the government purchase and then sell the crop, the NIDA contract is a very reasonable approximation of this treaty requirement.

Allowing bids on the NIDA contract every five years is a very reasonable accommodation of applying the treaty, as previously described, with allowing competition under Section 823(a)(1).

Respondent has proposed an alternative interpretation of the Single Convention based upon documents obtained from the United Kingdom agency that oversees marijuana production. (FOF-458-460) Based upon these pleadings, it appears that the United Kingdom's interpretation of the Single Convention (or at

least Respondent's interpretation) is that numerous marijuana cultivators can be registered, and the government will take "constructive" possession of the marijuana.

Such an interpretation is a virtual abandonment of the treaty's applicable provisions. It would allow virtually no regulation of marijuana cultivation. The Government's accommodation to the treaty is much more in accord with the spirit and the letter of the treaty than what is proposed by Respondent under Respondent's characterization of how the United Kingdom approaches the treaty.

Moreover, the Government is not compelled to follow the United Kingdom's system and interpretation of the treaty. There are over 100 signatories to the Single Convention, and each party may have unique ways in which it carries out its treaty obligations based upon that party's existing circumstances. Respondent apparently has found one party whose interpretation it believes is the definitive interpretation of the treaty, and, under Respondent's view, would allow multiple marijuana cultivators under "constructive" possession of the Government.. Under these circumstances, the Government's interpretation of the treaty under the existing circumstances is far superior to what Respondent has proposed.

Courts give deference to agencies' interpretations of treaties that the agencies enforce, as the courts would under agencies' interpretations of statutes that the agencies enforce. *Kolovrat v. Oregon*, 366 U.S. 187, 194-195 (1961)

(holding that a foreigner was entitled to an inheritance probated in Oregon based, in part, upon the interpretation of the treaty by the State Department); *O Centro Espirita Beneficiente Uniao Do Vegetal*, 342 F. 3d 1170,1193 (10th Cir. 2003) (majority opinion holding that the Religious Freedom Restoration Act (RFRA) overruled the Government's interpretation of the Single Convention because the RFRA was passed after the Single Convention; the dissent correctly explained that "... the interpretation of an international treaty by the United States agency charged with its negotiation and enforcement is entitled to 'great weight' from the courts.") Given this law, there is certainly no reason why DEA's and HHS's interpretation of the Single Convention as it relates to marijuana should not be given "great weight." (G-24)

ii. Factor 2

This factor pertains to the applicant's compliance with applicable State and local law. No parties have alleged or offered proof that Dr. Craker has not complied with any specific state or local statutes or regulations. 21 U.S.C. § 823(a)(2). Although Dr. Craker's sponsor, Dr. Doblin illegally abuses marijuana routinely and has caused marijuana to be diverted from a compassionate use patient to an analytical laboratory, these issues will be explored under Factor 6, since these violations are not necessarily violations of local or state law.[5]

5 Marijuana for non-medical use violates state laws even in those states where marijuana has been

iii. Factor 3

Under this factor Dr. Craker has the burden of proof to demonstrate that registering him would promote technical advances in the art of manufacturing marijuana, and the development of new substances derived from marijuana. 21 U.S.C. § 823(a)(3). Dr. Craker has not proposed any technical advances in cultivating marijuana, and he has not divulged any plans whatsoever to develop any new substances derived from marijuana. Nor has Dr. Craker revealed any plans how he would control potencies and alter constituents in marijuana.

Dr. Craker has no current or pending patents related to the cultivation of marijuana. (FOF-384) Dr. Craker's testimony that he would produce marijuana by controlling light regimes and controlling environmental factors was vague and nebulous. (FOF-386, 389) Equally unenlightening was his testimony that pruning and growing all female plants would have an effect on THC potencies because he then indicated that he had "not looked into those at depth ..." (FOF-393) Dr. Craker was not sure whether he would test for THC potency or outsource this function. (FOF-394)

Dr. Craker was not only unaware of any company doing research with a vaporizer delivery device for marijuana, he was also not qualified to judge such research. (FOF-383-384) Although Dr. Craker planned to distribute his marijuana to researchers, the plans he revealed went no farther than sending generic bulk

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"legalized" for "medical" use. The record does not indicate in what state Dr. Doblin abused marijuana.

marijuana to researchers. (FOF-394, 397)

What was most revealing was Dr. Craker's recitation of the cultivation process for marijuana during cross-examination. (FOF-391-396) The whole process, as described by Dr. Craker, was a generic cultivation process applicable to just about any horticultural product. *Id.*

Dr. Craker's lack of technical advances and the development of new substances, under this factor, should be compared to Dr. ElSohly's experience in this regard in order to highlight how Dr. Craker has failed to show anything of value under this factor. Dr. ElSohly has developed extraction processes, has isolated different components and has synthesized various cannabinoid components. (FOF-121, 128, 157-159) The Research Institute has the capability of cultivating and supplying various levels of THC potencies. (FOF-136, 137)

Dr. ElSohly has developed seedless marijuana based upon two different methods, and he can produce potencies up to 20%. (FOF-142, 160) He has cultivated marijuana outside that contains up to 15% THC. (FOF-149) He described two specific techniques to develop various potencies of marijuana-vegetative propagation and micro propagation. (FOF- 144) He has supplied placebo marijuana and is in the process of developing an improved placebo that will more closely mimic actual marijuana. (FOF-152, 156)

Dr. ElSohly has developed harvesting and storage techniques. (FOF-150-151, 163-164) He has developed an improved deseeding machine. (FOF-190-191)

He has procured various patents based upon his marijuana projects, and his abstracts demonstrate some of the unique features of his marijuana cultivation. (FOF-199-200) And Dr. ElSohly is conducting research on developing a marijuana extract product in conjunction with a pharmaceutical company, Mallinckrodt, for medicinal use. (FOF-203-207)

Dr. Craker has not even proposed to, much less planned to, do anything approaching what Dr. ElSohly has done at the Research Institute. Respondent, no doubt, will feature Dr. Craker's academic background and experience as a horticulturalist. But this background is insufficient because under Factor 3, the applicant must demonstrate technical advances and development of new substances in the particular substance for which he has applied, i.e. marijuana. Dr. Craker has not given any testimony how his background will translate into developing marijuana under Factor 3.

During the direct examination of Dr. Craker, Respondent inferred that supplying marijuana to researchers may lead to technological advancements. But Factor 3 applies to the applicant not some downstream researcher who would receive Dr. Craker's generic marijuana and might or might not develop a medicinal product. Moreover, this assertion is highly speculative even if Factor 3 is misconstrued under Respondent's interpretation.

iv. <u>Factor 4</u>

This factor pertains to an applicant's prior conviction record relating to the

manufacture, distribution or dispensing of controlled substances. 21 U.S.C. § 823(a)(4). Although Dr. Doblin has admitted to abusing marijuana and although Dr. Doblin was instrumental in diverting marijuana from a patient to an analytical laboratory for research, no convictions have been sought or obtained based upon these violations. Therefore, this factor does not apply. As noted previously, these incidents will be featured under Factor 6.

v. Factor 5

Under this factor Respondent has the burden of proof to demonstrate past experience in the manufacture of controlled substances, and the existence in the establishment of effective controls against diversion. 21 U.S.C. § 823(a)(5). Although the Government does not take issue with Dr. Craker as to the latter requirement, the Government asserts that the application is woefully deficient because of Dr. Craker's lack of experience.

When pharmaceutical drug companies seek applications to import or manufacture Schedule II controlled substances, such applicants always have some experience in the manufacture of some controlled substances. And this factor is weighed in their favor in determining whether or not to grant the applications. *Johnson Matthey; Approval of Registration*, 60 Fed. Reg. at 26,052; *Manufacture of Controlled Substances*, 61 Fed. Reg. at 37,080; *Chattem Chemicals, Inc.; Grant of Registration to Import Schedule II Substances*, 71 Fed. Reg. at 9,838.

Dr. Craker admitted that he had no past experience growing marijuana or

handling any other controlled substances for that matter. (FOF-387) Indeed, one reason Dr. Craker chose not to compete by bidding on the NIDA contract was based upon his lack of experience. (FOF-389)

No doubt, Respondent will argue the relevant experience that Dr. Craker has as a professor of horticulture. But this argument should be rejected because Factor 5, as was the case for Factor 3, refers explicitly to controlled substances. Moreover, as a matter of fact, Dr. Craker submitted no convincing evidence how his academic experience would translate into a larger scale cultivation of marijuana. The Government's argument under Factor 3 also supports the latter premise.

vi. Factor 6

Under this factor, DEA should consider the conduct of Dr. Doblin as it relates to his controlled substance violations.

Dr. Doblin's is not just a peripheral player in this application, so his conducted cannot be discounted. Dr. Doblin approached Dr. Craker to ask Dr. Craker to submit an application. (FOF-372, 380) Dr. Doblin assisted Dr. Craker in supplying the answers to the bulk manufacturers' questions on the DEA application. (FOF-398) MAPS, through Dr. Doblin, would designate the researchers who would receive marijuana from Dr. Craker. (FOF-372) Dr. Doblin would work with FDA, devise a strategy and find the researchers who would use Dr. Craker's marijuana. *Id.* And Dr. Doblin would direct Dr. Craker to produce

certain potencies of marijuana and gave Dr. Craker an estimate of 25 pounds for the initial marijuana crop. (FOF-398)

Dr. Doblin believes that marijuana should have the same legal status as tobacco, coffee and sugar. (FOF-355) Dr. Doblin's belief in this regard is not just theoretical; he has abused marijuana on a recreational basis ever since he was in college in 1971. (FOF-356) He abused marijuana in this manner the week prior to the date of his testimony. *Id.* Dr. Doblin's response to the question of where he obtained the marijuana he abused was flippant, and such an answer indicates that he has a cavalier attitude towards marijuana regulation. (FOF-357)

Another very disturbing incident pertains to Dr. Doblin diverting marijuana, intended for consumption by an experimental use patient, to Chemic, Inc., a DEA registered analytical laboratory; Chemic was to use this marijuana in researching a vaporizer. (FOF-364) Dr. Doblin directed a compassionate use patient to divert his marijuana to an analytical laboratory when the patient was not registered as a distributor and Chemic was not authorized to receive such marijuana. 21 U.S.C. § 822(e); 21 U.S.C. § 823(b). Dr. Doblin's testimony regarding this incident was elusive and not particularly candid. (FOF-365-371) This incident demonstrates that Dr. Doblin would not be adverse to going outside DEA regulations to accomplish his purposes.

B. Respondent's contention that any marijuana researcher should not have to abide by the May 1999 HHS Policy Statement

a. How the peer review system is designed

When a researcher needs marijuana, he must obtain it from NIDA's drug supply, and he cannot obtain it until he has an FDA IND approved and has his protocol approved by an ad hoc HHS review committee. (FOF-284) For researchers who do not want grants, they must submit their protocols to an ad hoc PHS review committee, consisting of various experts from various HHS agencies as well as the private sector. (FOF-285-286, 293) If a researcher also seeks Government grants, then the ad hoc committee from the NIH performs the same type of protocol review as does the PHS committee. (FOF-287) And even researchers who seek NIDA marijuana for non medical use of marijuana must undergo a protocol review similar to the PHS committee's review. (FOF-288)

The ad hoc peer review by PHS, NIH or a peer-review committee for researchers who seek to do non-medical research with marijuana is not required for researchers who obtain the research drugs from other sources. (FOF-289) Some Schedule I controlled substances can be obtained from non government sources. (FOF-297)

The May 1999 HHS policy statement described the process for PHS protocol reviews. (FOF-292, 294-295) Dr. Gust noted that it was not difficult to have protocols approved because the scientific "bar" was low and any project with scientific merit would be approved. (FOF-300) If a protocol is initially denied, it

can be resubmitted. (FOF-301)

Approved NIH protocols (for researchers seeking Government grants) are prioritized on a scale of scientific merit; those with the highest scores are awarded first with available funds. (FOF-299) The May 1999 HHS policy statement made available marijuana to researchers who were willing to reimburse the Government for the cost of the marijuana. (FOF-307)

Dr. Gust explained that the PHS protocol process was not a superfluous process to the FDA IND approval because FDA was looking primarily at safety issues while the PHS protocol review was primarily looking at scientific merit. (FOF-290) Respondent's pharmaceutical expert, Dr. Martin, reinforced this testimony by noting that the FDA's primary responsibility is to assure public safety and not to assure that new drugs are developed. (FOF-18)

b. Chemic's protocol rejected by the PHS committee

Dr. Doblin arranged to have Chemic, Inc., a DEA-registered analytical laboratory, test a vaporizer as a marijuana delivery system instead of smoking. (FOF-327) Dr. Doblin, *inter alia*, sought to have Chemic obtain NIDA marijuana for the vaporizer experiments; eventually, the PHS committee rejected Chemic's protocol. (FOF-328-329)

Dr. Doblin believed that Chemic would not submit a new protocol but would either appeal to the PHS committee to accept the protocol or challenge the PHS committee's rejection of the protocol in a court. (FOF-330)

c. Respondent's fallacious contention that Dr. Craker should be registered in order to circumvent the May 1999 HHS policy statement and protocol reviews

Respondent's position is that Dr. Craker's application should be granted so that Dr. Craker can circumvent the May 1999 HHS policy and supply marijuana to any researcher that wants it as long as the researcher has a DEA registration and an approved FDA IND. Respondent maintains that other Schedule I controlled substances can be researched without the necessity of needing a separate protocol review from the PHS; marijuana is subject to discrimination on this basis. And Respondent claims that the PHS protocol review is an unnecessary hurdle because it duplicates the HHS process.

1. Respondent's contention fails as a matter of law

If Dr. Craker is registered, Respondent wants DEA to allow Dr. Craker to supply researchers with marijuana without having to go through any PHS or ad hoc committee protocols. In other words, Respondent is inviting DEA to violate HHS policy. This proposition is an invitation DEA should unequivocally decline because DEA has absolutely no legal authority to do so.

In *Food and Drug Administration v. Brown and Williamson Tobacco Corporation*, 529 U.S. 120 (2000), FDA promulgated rules, under the Food, Drug and Cosmetic Act, which regulated the sales of tobacco products to minors. After an exhaustive review of the legislation relating to tobacco, the Court, by a five-to-four margin, held that FDA had no jurisdiction over tobacco products and nullified all the FDA regulations. In *Gonzales v. Oregon*, 126 S. Ct. 904 (2006), the

Supreme Court struck down a DEA policy statement, which indicated that DEA would seek to revoke DEA registrations of any physicians who used controlled substances to assist suicide including those physicians who would do so in compliance with the Oregon Death with Dignity Act. The Court reasoned, in a six-to-three decision, that the Controlled Substances Act did not give DEA jurisdiction to promulgate a policy that declares as illegitimate a medical standard for treatment of patients that is authorized under state law.

Given these two cases and basic administrative law, there is no question that DEA has no legal authority to overturn the May 1999 HHS policy statement, even if the policy were unreasonable nor within HHS's legal authority to promulgate. Any challenge by Respondent must be against HHS, not DEA. Respondent's attempt to do an "end around" by having DEA register Dr. Craker to, *ipso facto*, overrule, as a matter of law, the HHS May 1999 policy statement. Most assuredly, DEA is not the agency to test the legality of what HHS does.

2. Respondent's contention fails as a matter of fact

As a factual matter, this argument also fails. Both Dr. Doblin and Dr. Craker testified that no researchers are "lined up" just waiting for Dr. Craker to become registered. (FOF-344, 380-382) Although Chemic had a protocol rejected, it has an opportunity to resubmit its protocol or persuade the PHS committee that its protocol is not deficient. Chemic should exhaust its remedies with the PHS, and not use DEA as a proxy to override HHS policy.

In any event, no one on behalf of Respondent has offered any credible testimony that the PHS committee's rejection of Chemic's protocol was not based on sound science or reasoning. Indeed, not one of Respondent's witnesses were qualified to offer such an expert opinion. In light of this fact, the proposition to have DEA unilaterally overrule another agency's policy is even more dubious.

Moreover, the record does not support Respondent's contention that the PHS committee protocol review is superfluous to the FDA IND. Yet both Dr. Gust and Dr. Martin testified that the FDA review is primarily about safety. (FOF-18, 290) As Dr. Gust explained, a pharmaceutical company makes its own determination whether its research has scientific merit while the PHS research protocol reviews are an alternative method to ensuring that the studies have a sound basis in science. (FOF-290) The HHS policy in this regard may make it more difficult for marijuana researchers (as well as other Schedule I controlled substance researchers), but the policy is sound. In other words, even if DEA had any authority to overturn the HHS policy, it would have no basis to do so because the policy is permissible and reasonable under the circumstances.[6]

C. Respondent's contention that Dr. Craker should be registered in the event of an emergency

Respondent suggested that Dr. Craker's application should be granted in case there was an emergency at the Research Institute of the University of

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6 The Government argued previously herein that the HHS policy also was reasonable under the Single Convention. So, if DEA had the legal authority to overrule the HHS policy in this regard, it would not

Mississippi. Dr. Craker's registration is not necessary under this argument based upon DEA law and policy. Moreover, any emergency would not be ameliorated by the registration of Dr. Craker whose operation would be limited to indoor cultivation.

As previously noted under the Government's argument advocating that Dr. Craker's DEA registration would be a contingent registration, it has long been DEA's policy not to register those who want the registration as a "shelf registration." In *Registration of Importers; Statement of Policy and Interpretation*, 40 Fed. Reg. 43,742 (1975), DEA noted that a number of firms previously obtained registrations as Schedule I and II controlled substance importers and that such registration were not in current use but only to be used if there were an emergency. In this policy statement, DEA announced that it would no longer register any companies on this basis because 21 U.S.C. § 952(a)(2)(A). such controlled substances could be **imported** on an expedited basis. The policy statement concluded in regard to the existing shelf-life registrations that "... such a 'contingent reserve' of registrants is unnecessary and also, administratively burdensome." 40 Fed. Reg. at 43,746. Therefore, there is no basis to register Dr. Craker because of a possible emergency at the Research Institute.

Respondent's argument also should be rejected as a matter of fact. Dr. Craker plans to grow marijuana only in an indoor facility. (FOF-386) Even if Dr.

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prevail, since the HHS interpretation of the Single Convention is reasonable.

Craker had planned to grow outdoors, the climate limitations in Massachusetts would make such outdoor cultivation much more uncertain than in Mississippi because, as Dr. ElSohly testified, marijuana crops can be adversely affected by temperatures of 25° or less. (FOF-140)[7] In addition, Dr. ElSohly testified that the Research Institute could expand its indoor facility if need be. (FOF-141)

D. Exclusion of DEA final orders from evidence

During the hearing, the Government sought to introduce into evidence two final orders, *The Church of the Living Tree: Denial of Application*, 68 Fed. Reg. 17,403 (2003) (G-61), and *Marion "Molly" Fry, M.D; Revocation of Registration*, 67 Fed. Reg. 78,015 (2002) (G-63). (Tr.-1789-1790; Tr.-1792-1794). Respondent objected to the admission of these final orders on the basis of relevancy. (Tr.-1793, l. 15-19) The ALJ ruled that these final orders were not admissible. (Tr.-1794, l. 1-18) But the ruling was not based on relevance; the ALJ ruled that the final orders were inadmissible because they were not based upon an adjudicatory record but were issued on the basis of the investigative file because the applicant and registrant, respectively, waived their rights to an adjudicatory hearing. 21 C.F.R. §§ 1301.43(d) and (e). (Tr.-1794-1795, l. 19-22, 1-5)

The Government requests that the ALJ reverse her ruling and admit these exhibits for the following reasons. There is no question that hearsay is admissible.

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7 Dr. ElSohly testified the growing season is from mid-April to September or November. (FOF-140). Since Dr. Craker never offered plans to grow marijuana outdoors, there is nothing in the record to indicate the marijuana growing season in Massachusetts.

Margaret E. Sarver, M.D.; Suspension of Registration; Reinstatement with Restrictions, 61 Fed. Reg. 57,896, 57,899 (1996), holding that uncorroborated hearsay is admissible in DEA administrative proceedings. See also *Klinestiver v. Drug Enforcement Administration*, 606 F. 2d 1128 (D.C. Cir. 1979), which upheld the admissibility of hearsay in DEA adjudicative hearings.

The exclusion from evidence of the final orders under these circumstances should not be an exception to DEA's general rule to admit hearsay. Indeed, these final orders have more reliability than much of the evidence that is admitted. The final orders are very analogous to the hearsay exception under Fed. R. Ev. 803(8), which allows public records and reports to be admitted as an exception to the hearsay rule. See *Beech Aircraft Corp., v. Rainey*, 488 U.S. 153, 170 (1988), holding that in a suit against an aircraft manufacture based upon an aircraft crash, a Judge Advocate General Report that gave factual conclusions about the causes of the crash was admissible under Fed. R. Evid. 803(8)(C).

Moreover, these final orders should be admitted more on the basis of the general information they provided about marijuana, i.e., the extent of abuse and the dangers and social costs of marijuana abuse. Consequently, the basis of admissibility is predicated on legislative, and not case-specific adjudicative, facts. In any event, Respondent was not precluded from challenging such evidence on this basis.

E. "Impeachment" of Dr. Gust

Respondent filed a "Motion to Admit Additional Exhibits in Rebuttal", dated January 5, 2006. This motion noted, *inter alia*, that Dr. Gust testified that there was only a "handful" of Schedule I controlled substances available from other sources (other than NIDA) for researchers. (Tr.-1644, l. 6-12) Respondent introduced a post-hearing document, which indicated that a number of companies had 30 Schedule I controlled substances commercially available to researchers. (R-59; Motion to Admit Additional Exhibits in Rebuttal at pg. 5)

Respondent seeks to highlight the argument that marijuana is "singled out" as a Schedule I controlled substance because it is the only controlled substance that can be obtained through NIDA and, thus, subject to some type of HHS protocol review. When Dr. Gust testified that there were only a "handful" of controlled substances available from the private sector, i.e., most Schedule I controlled substances must be obtained through NIDA, such testimony diminished Respondent's premise.

In response to the admission of Respondent Exhibit 59, the Government requested the ALJ to take administrative notice that there are 125 controlled substances in Schedule I. The ALJ did so in her Memorandum to Counsel and Ruling, dated January 24, 2006. (pg. 3)

The impeachment of Dr. Gust in this regard is marginal to say the least. Respondent is relegated to arguing that 30 Schedule I controlled substances are

more than a "handful." In the context of the fact that there are 125 different Schedule I controlled substances, this impeachment becomes even more marginal.

F. Conclusion

Dr. Craker's application should be denied under Factor 1 based upon the following. Respondent's argument that marijuana supplied to researchers by the Research Institute at the University of Mississippi is inferior in quality and potency is based on outdated and marginal complaints. Despite having the burden of proof, Respondent did not call one researcher to testify about the "inferior" quality of NIDA marijuana. Respondent has not come close in its burden to demonstrate this proposition. Indeed, this argument is, in reality, a pretext to rationalize the "need" for another marijuana supplier. In any event, the record is not in dispute; the CMCR researchers have not had their research studies curtailed at all due to any "deficiencies" in the marijuana.

Another glaring deficiency in Respondent's case is that Respondent has not offered any evidence of how Dr. Craker would "cure" these problems, assuming there were any problems to cure. Rather, it was Dr. ElSohly who convincingly testified that the Research Institute has more than ample capability and ability to adjust its operation to provide any level of potency of marijuana, to deseed and de-stem marijuana, and to adjust its operation in any way needed to accommodate any existing or potential researchers.

The record is also very clear that Dr. Craker's registration would be nothing

more than a contingent or "shelf" registration. Respondent's premise is that when pharmaceutical companies know that there is a ready source of supply, they will then file INDs to develop a marijuana plant material as a pharmaceutical drug.

First, there was more than ample testimony that a ready source of supply is not the only hurdle that a pharmaceutical company would have to overcome. Aside from the costs and the regulatory obstacles, there are the extra complexities to overcome in dealing with botanicals as both Dr. Auslander and Dr. Voth noted. And Dr. Craker is proposing to limit his distribution to the plant material only, the least likely part of marijuana, as opposed to extracts, that would be developed as a pharmaceutical medicine.

Second, while the record is uncertain that Dr. Craker would be able to supply marijuana to a pharmaceutical drug developer company, the record is very clear that the Research Institute has the ability to do so.

Third, even if one discounted the latter two arguments, Respondent has not mentioned one pharmaceutical company that has expressed any interest whatsoever in developing a pharmaceutical drug from marijuana plant material. Even if Respondent had demonstrated that there were no significant barriers to developing marijuana as a pharmaceutical drug, the fact is that there is no pharmaceutical company interested in doing so.

Dr. Doblin's testimony that MAPS could become such a pharmaceutical company could hardly overcome these hurdles. It is much too speculative to

register Dr. Craker on the basis that some day MAPS might become a pharmaceutical company by building the infrastructure to accommodate all the commercial and regulatory requirements to compete in the pharmaceutical industry.

"Competition" as that term is used in 21 U.S.C. § 823(a)(1) is provided by the bidding system for the NIDA contract. Under the circumstances, defining "competition" in this manner is a very reasonable alternative compared to treating marijuana as a large-scale bulk manufacturing pharmaceutical where DEA registers several manufacturers and importers. Moreover, the bidding system is the best definition of "competition" in order to accommodate the Single Convention and the May 1999 HHS policy, which the DEA has no authority to overturn by registering another marijuana cultivator.

Even if DEA had the statutory authority to overturn the HHS policy, Respondent has presented no cogent evidence or reason why DEA would ever want to overturn the policy. Dr. Craker is seeking to distribute marijuana to researchers, as yet unidentified, who would undergo no PHS protocol review, i.e., researchers who are marginal and more likely to divert or abuse their privileges unlike the current marijuana researchers. Dr. Craker seeks to distribute plant marijuana to researchers and developers who ostensibly would be using and developing plant material, which is the most commonly abused form of marijuana.

Under Factor 3, Dr. Craker's application should be denied. Respondent has

not offered any proof whatsoever, that Dr. Craker would promote technical advances in the art of cultivating marijuana or advancing in way the development of new strands or extracts of marijuana under Factor 3. 21 U.S.C. § 823(a)(3).

Under Factor 5, the application should be denied because Dr. Craker has no past experience in manufacturing any controlled substances, much less marijuana as set forth. 21 U.S.C. § 823(a)(5).

Under Factor 6, the application should be denied. Dr. Doblin, the sponsor and driving force behind Dr. Craker's application, not only advocates marijuana being treated like alcohol or coffee, he also is a chronic abuser of marijuana. Moreover, Dr. Doblin has demonstrated that he will act outside the closed loop and circumvent DEA regulations when he believes he needs to do so, as demonstrated by his part in diverting marijuana intended for a patient to a laboratory for experimentation.

Dr. Doblin opined, "... I think the Government should be penalized for blocking medical marijuana research for 30 years." (FOF-358; Tr.-634, l. 7-13) Even if the record demonstrated that DEA or HHS "blocked" legitimate research (which it most assuredly does not), the purpose of these proceedings is to protect the public interest rather than "penalize" the Government. There are ample grounds to deny Dr. Craker's application either under Factors 1, 3, 5 or 6. When these factors are considered together and when Respondent has the burden of proof, there is really no realistic alternative but to deny Dr. Craker's application.

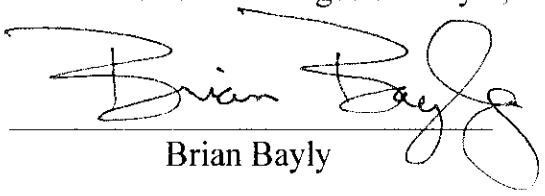
Respectfully submitted,

Brian Bayly
Attorney
Office of Chief Counsel

DATED: May 8, 2006

CERTIFICATE OF SERVICE

On May 8, 2006, I caused a copy of the foregoing to be mailed by Federal Express or courier, postage prepaid, to counsel for Respondent, Julie Carpenter, Esq., Jenner & Block, LLP, 601 13th Street, N.W., Washington, D.C. 20005. This is to further certify that one original and two copies of the foregoing were delivered by hand to the DEA Office of Administrative Law Judges on May 8, 2006.



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