UNITED STATES DEPARTMENT OF JUSTICE
DRUG ENFORCEMENT ADMINISTRATION

IN THE MATTER OF	**Docket No. 05-16**
Lyle E. Craker, Ph.D.	

GOVERNMENT'S PREHEARING STATEMENT [INITIAL]

In the Matter of Lyle E. Craker, Ph. D. ("Dr. Craker" or "University of Massachusetts, Amherst")

Pursuant to the February 8, 2005 Order of the Administrative Law Judge, the United States Department of Justice, Drug Enforcement Administration, by and through the undersigned attorney, hereby submits the following prehearing statement.

ISSUE

Whether the Drug Enforcement Administration (DEA) should deny Dr. Craker's application to manufacture (cultivate) marijuana, a Schedule I hallucinogenic controlled substance, for reason that DEA has not determined that such registration would be consistent with the "public interest," as that term is defined in 21 U.S.C. § 823(a), or with obligations under international treaties, conventions, or protocols in effect on May 1, 1971.

PROPOSED STIPULATIONS AND ADMISSIONS OF FACT

1. Marijuana is a Schedule I hallucinogenic controlled substance under 21 C.F.R. § 1308.11(d)(20) and 21 U.S.C. § 812(c)(10) (2004).

2. Marijuana has a high potential for abuse. 21 U.S.C. § 812(b)(1)(A).

3. Marijuana has no currently accepted medical use in treatment in the United States. 21 U.S.C. § 812(b)(1)(B).

4. There is a lack of accepted safety for use of marijuana under medical supervision. 21 U.S.C. § 812(b)(1)(C).

5. Dronabinol (synthetic), in sesame oil and encapsulated in a soft gelatin capsule in a U.S. Food and Drug Administration (FDA) approved product, is a Schedule III hallucinogenic controlled substance. 21 C.F.R. § 1308.13(g)(1). Marinol is a brand of this Schedule III controlled substance, dronabinol. *Physician's Desk Reference*, 56th Edition, Medical Economics Company, Montvale, New Jersey (2002), pg. 3325.

6. Marinol is indicated for the treatment of: (1) anorexia associated with weight loss in patients with Aids; and (2) nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. *Physician's Desk Reference*, 56th Edition, *Id.*

PROPOSED WITNESSES

Helen Kaupang, Staff Coordinator
Domestic Drug Unit (ODOD)
DEA Headquarters
DEA Office of Diversion
Arlington, VA 22201

Mahmoud A. ElSohly, Ph.D.
National Center for Natural Products Research
University of Mississippi
Oxford, Mississippi

Steve Gust, Ph. D.
National Institute of Drug Abuse
U.S. Department of Health and Human Services
Bethesda, Maryland

Matthew Strait
Chemical and Drug Unit (ODE)
DEA Headquarters
DEA Office of Diversion
Arlington, VA 22201

Representative of the Public Health Services' Committee
U.S. Department of Health and Human Services
Bethesda, Maryland

Representative of the Research Triangle Institute
Research Triangle Institute
Research Triangle Park, North Carolina

Proposed Testimony of DEA Staff Coordinator Helen Kaupang

Ms. Kaupang will testify about her jobs, experience, training and education while with DEA. She will explain her past and present positions with DEA.

She will testify that on October 8, 2003, a meeting was held at the National Center for Natural Products Research (the Center) on the U. Miss. campus. In attendance at this meeting were Larry Walker, Ph.D., Center Director, Walter G. Chambliss, Ph.D., Associate Director of the Center, and Mahmoud A. ElSohly, Ph.D., Research Professor.

Ms. Kaupang will explain the DEA process for transferring marijuana from U. Miss. to the researcher. The researched fills out and submits a DEA 222 order form to NIDA. NIDA logs in the 222 order-form, endorses it and sends it to the Research Triangle Institute (RTI), the institute that processes marijuana for research use. (The role of RTI is explained under Ms. Kaupang's testimony *infra*.) NIDA informs U. Miss. that there is a pending order, and then U.Miss. logs onto NIDA's secure computer tracking system to obtain the order. U. Miss. then sends the researcher a letter with an "Order and Assurance Form" and a "Release and Indemnity Agreement." When the researcher signs and sends these forms to U. Miss., along with payment if applicable, U. Miss. logs onto the NIDA secure computer system to note that U. Miss. has received these items from the researcher. U. Miss. then releases the order and contacts RTI to have RTI ship the order.

Ms. Kaupang will explain that after that Dr. Craker submitted his application to manufacture marijuana, DEA sent Dr. Craker a list of standardized questions for bulk manufacturers. (G-2) Dr. Craker then re-submitted his application with answers to these questions. (G-3) The answers indicated, *inter alia*, that Dr. Craker wanted to cultivate marijuana "for federally-approved uses only, including analytical, pre-clinical and clinical research" and "... to develop the marijuana plant in an FDA-approved prescription medicine." (G-3)

Research Triangle Institute (RTI)[1]

On December 16, 2003, a meeting was held between DEA personnel, Mr. Strait, Ms. Kaupang, and Diversion Investigators Gwen Kittrell and Michael Callan, and Research Triangle Institute (RTI) personnel, Alan Stapler, Vice President of the Health Sciences Group, Brian Thomas, Ph. D., Director of the Bioanalytical Chemistry Center, Kenneth H. Davis, Jr., Senior Program Director of the Bioanalytical Chemistry Center, and Victor L. Parker, Jr., Supervisor of Shipping and Drug Supply of the Bioanalytical Chemistry Center. The meeting was held at RTI, Research Triangle Park, North Carolina. The purpose of the meeting was for DEA personnel to interview individuals working on the National Institute on Drug Abuse Marijuana Project (NIDA M Project) in conjunction with the University of Mississippi. The DEA inquiry pertained to the quantity, quality and availability of marijuana through NIDA for medical and scientific research.

RTI is a non-profit independent organization involved in scientific research and technology development in order to improve the human condition. It 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 a Schedule II-V researcher. All

[1] Dr. ElSohly also will testify about some or all of the information related to RTI as set forth under this part of the proposed testimony of Matthew Strait.

registrations are maintained by the Health Sciences Group and are overseen by Kenneth Davis, Jr. (Mr. Davis).

Since 1968, RTI had been involved in the NIDA M Project by producing and distributing marijuana cigarettes to FDA/DEA approved researchers as well as to patients in the experimental use program. The bulk marijuana for rolling marijuana cigarettes has been supplied by U. Miss. 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 Project.

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.

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.

The production process takes place in a warehouse building on the RTI campus. During the entire production process, from the time the plant material is removed from the vault and taken to the warehouse until the cigarette trays are returned to the vault for drying and packing, the operation is manned and supervised twenty-four hours a day.

A total of 32 batches of machine rolled marijuana cigarettes have been produced by RTI since the beginning of the NIDA M Project. These 32 batches have provided for the legitimate scientific requirements of the United States since 1974. Production is always governed by what NIDA needs and requests.

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 not appropriate for mechanical rolling. Recent consultations with their tobacco industry counterparts have led RTI to believe that it could now produce machine rolled cigarettes at 8% THC if necessary. Whether or not the mechanical process works, an adequate and uninterrupted supply of high potency marijuana cigarettes can be manufactured using a hand-rolled technique if necessary. On occasion, a researcher requests RTI to ship bulk material to researchers, but that is a relatively rare occurrence.

Proposed Testimony of Mahmoud A. ElSohly, Ph.D. (Dr. ElSohly)

Dr. ElSohly will testify about his academic background and credentials in relation to his current position as the research professor and Professor of Pharmaceutics at the School of Pharmacy Research, and Director of the National Institute of Drug Abuse (NIDA) Marijuana Project at the University of Mississippi (U. Miss.). he will present and testify about his C.V. He will give an overview of the University of Mississippi's history regarding the cultivation of marijuana and extraction of THC, which began in 1968. (Dr. ElSohly began his work at this program in 1976 but is aware of the history of the program since it commenced in 1968.)

Dr. ElSohly will testify that he submitted comments and objections to Dr. Craker's application when Dr. Craker's application was published in the *Federal Register*, which invited comments and objections to the application. (G-5) Dr. ElSohly will further elucidate his comments and objections to the application.

Dr. ElSohly will explain that DEA initially registered the University of Mississippi, Research Institute of Pharmaceutical Sciences, School of Pharmacy, as an analytical lab registration.

On February 5, 2002, DEA granted a bulk manufacturer registration to the U. Miss., National Center for Natural Product Research NIDA Marijuana Project (NIDA M Project). The M Project has always been funded under a contract with NIDA. The contract was changed from a three year to a five-year commitment during the 1998/1999 open competition. The current contract was scheduled to

expire on November 8, 2004, but was extended, without additional funding, until March 1, 2005. Dr. ElSohly will further explain that the contract was opened up for bidding by NIDA in 2004, U. Miss., through Dr. ElSoly, bid on the contract and the contract award is still pending.

The NIDA contract requires U. Miss. (or the successful bidder who is awarded the contract) to cultivate and process marijuana, which is used to make bulk material and cigarettes under "Good Manufacturing Practices" (GMP) guidelines, which are required by the FDA and to conduct potency studies on seized marijuana plant material with quarterly reports to NIDA and DEA. The U. Miss. currently conducts research on marijuana for plant propagation, indoor cultivation, potency studies, placebo plant material development and product development.

Since its inception, the marijuana potency program has analyzed more than 50,000 samples seized by U.S. law enforcement. NIDA's contract requires the analysis of 100 samples per month (1,200 per year). U. Miss. has been analyzing all samples submitted to the program, which exceeded the required amount and which includes analysis of up to 4000 or more samples a year.

Prior to 1999, NIDA awarded two contracts- one was to U. Miss. for cultivation and potency studies; the second contract was awarded to the Research Triangle Institute (RTI) in North Carolina for the production and distribution of marijuana cigarettes to researchers (after NIDA approval). In 1999, a single NIDA contract was awarded, which included all activities- cultivation,

distribution, potency studies and some THC extraction. The U. Miss. subcontracted to RTI to cigarette manufacturing and distributing portion of the contract.

NIDA, in conjunction with U. Miss. (or whoever is awarded the next contract), decides how much marijuana will be produced in any given year. The U. Miss. has a 12-acre site on which it may cultivate marijuana. Since the beginning of the contract in 1968, the U. Miss. has cultivated several marijuana crops for NIDA and NIDA's predecessor agency, the NIMH. The U. Miss. recently has exercised its option not to grow any marijuana crops because of the massive inventory of marijuana at the U. Miss. storage facility.

Currently, the U. Miss. has available for NIDA different batches of marijuana that have various potencies. Some of this material is stored under freezer conditions to preserve the THC content.

The U. Miss. M. Project maintains DEA registrations for bulk manufacturing as well as other registrations relating to marijuana. Dr. ElSohly will testify about and verify these registrations.

The U. Miss. has approximately ten permanent employees who work on the NIDA M Project. When a marijuana crop has to be cultivated, additional part-time employees are hired on an hourly basis as needed.

Under the NIDA contract, U. Miss. (or whoever will be awarded the 2004 contract) is obligated to provide, and has provided, NIDA with research materials with specific potencies of marijuana. Under the NIDA contract, the U. Miss. has

produced for NIDA marijuana of various potencies ranging from slightly over 1 % to 10% or higher. The U. Miss. also is capable of producing specialized product such as sensilla marijuana. During the past two years, the U. Miss. has conducted some extractions and has purified THC for NIDA.

Because of some researchers' complaints about the occasional presence of seeds and/or small stem particles in the marijuana cigarettes, the U. Miss. invested in and installed a de-seeding machine prior to the 2001 growing season, which eliminated any seeds and stem pieces.

In the current inventory at the U. Miss. there is in excess of 1,500 kilograms of marijuana. This marijuana has potencies ranging from slightly over 1 % to more than 10% THC content. Given this supply and the capabilities of the U. Miss., there is a sufficient supply to meet the researchers' needs for some time to come.

Proposed Testimony of Steve Gust, Ph. D.

Dr. Gust is Special Assistant to the Director, National Institute on Drug Abuse, National Institutes of Health. He will testify as to his education, training, experience, and duties, give background information on the US Government's contract to provide marijuana for medical and research purposes. Dr. Gust currently serves as the program official with responsibility for monitoring the current contract with the University of Mississippi (U. Miss.).

The first contract to grow and distribute marijuana on behalf of the US Government was awarded in 1968 and was administered at the time by the

National Institute of Mental Health. Since that time, there has been nine contract cycles for cannabis production, the manufacture of cannabis cigarettes, analysis of cannabis samples, storage of preparation and bulk samples, and shipment of marijuana to researchers. For most of the period between 1968 and the present, the U. Miss. was awarded a contract for growing and processing bulk marijuana, and the Research Triangle Institute (RTI) was awarded a separate contract for the manufacture of marijuana cigarettes, analyzing, storage, and shipment. As of 1999, the two contracts were merged into one, and the U. Miss. has been the prime contractor since that time. RTI has continued to provide services under subcontract to U. Miss. The current contract will end on February 28, 2005. A new contract is scheduled to be awarded on March 1, 2005, and expires on March 1, 2010. The U. Miss. was the successful bidder for the new contract, however it should be noted that the procurement was open to any and all bidders. Dr. Gust will testify that he asked specifically for the notice of the bidding for this contract be sent to Dr. Craker.

In 1999, the Department of Health and Human Services (HHS) created the PHS committee. The PHS Committee is comprised of individual researchers that are experts in various fields and includes National Institute of Health (NIH) staff members and other health agencies such as the FDA. The PHS committee makes recommendations regarding the scientific merit of research proposals. The PHS has had responsibility for this since 1999 when the Department of Health and Human Services established the committee as part of a new policy to make

marijuana available for bona fide research on potential medical applications. This function was provided by PHS since NIDA was primarily designed to study drug abuse and the FDA, through the Investigational New Drug (IND) Application process, was designed to study primarily drug safety.

Furthermore, when an IND (Investigational New Drug application) is approved, FDA requires the researcher and the manufacturer of the controlled substance with various reporting responsibilities to insure public safety, such as adverse effects from use and annual progress reports. NIDA is the agency charged with providing the researcher with the controlled substance. Therefore, HHS determined that PHS review and approval would be a prerequisite before NIDA could release the marijuana. PHS's approval is independent of NIDA, although NIDA staff participate in the review process.

In addition, approval by the PHS committee, researchers are required to apply to the FDA for an IND (Investigational New Drug application) and to register with the DEA before final shipment of marijuana can occur.

NIDA requires the Contractor to develop a variety of marijuana types for research purposes, including a high-THC content product using various agricultural techniques to improve THC content. The Contractor must develop standardized cigarettes for pre-clinical and clinical research programs, and develop methodology for the preparation of small batches of cigarettes of specified delta-9-THC concentrations (presumably high potency), which may include hand-rolled cigarettes.

U. Miss. is obligated to analyze up to 1200 samples of seized marijuana to measure cannabinoid content per year. U. Miss. has actually been analyzing 2000 to 4000 samples a year. This information has allowed NIDA to monitor the THC content of "street" marijuana and to use that information to determine the range of THC levels required for its research grade marijuana produced at the U. Miss. facility. In general, the THC content of the marijuana available from the U. Miss. facility has closely matched the average THC content of the seized marijuana samples and therefore is believed to be representative of the marijuana generally available on the street.

Dr. Gust will further testify that NIDA never has received formal complaints about the quality of the marijuana it cultivates and distributes. He will further explain that some sticks, stems and seeds are expected in the product. He noted that press articles maintain that the marijuana is low potency. Dr. Gust explained that the Contractor is obligated to produce a higher potency marijuana than that which has been historically produced, and NIDA has taken extraordinary steps to ensure that the approved researchers' needs are met. Only one researcher group, CMCR, requested a higher potency than the 4% than NIDA has historically produced.

Dr. Gust will explain that a researcher would know what maximum potency is available by the results of discussions between NIDA, U. Miss. or RTI and the individual researcher. NIDA has also required the contractor to develop small amounts of higher potency materials for research purposes and to conduct research

on developing more stable storage mechanisms for such potent marijuana. (The higher the marijuana potency, the more rapidly it degrades.)

Dr. Gust disagreed with the marijuana legalization advocates who claim that low potency (i.e., low THC content) indicates low quality of marijuana that is of poor quality for medical research. Dr. Gust explained the latter argument was incorrect because it confused the term "dose" with the term "potency." Dr. Gust referred to the *Pharmaceutical Basis of Therapeutics*, which stated that a drug's potency is relatively unimportant in the clinical use of the drugs as long as the required dose can be administered conveniently and there is not toxicity related to the chemical structure of the drug. While there is no known toxic THC dose, high doses potentially delivered through high potency marijuana is a concern since the dose obtained is more difficult to control when smoking or administering a high potency marijuana vs. a lower potency marijuana. In general, the THC content (or potency) is not a relevant concern since a researcher could easily increase the dose achieved by for example, increasing the number of puffs of a cigarette or amount of time smoke is held in the lungs.

The potency issue is also a concern when marijuana in ingested by routes other than smoking a cigarette, such as ingestion. Some have argued that higher potency marijuana is less toxic via the smoking route since fewer by products would be ingested when smoking. There would be reduced exposure to toxins in the smoke when smoking a high potency cigarette but there is reason to be concerned about the hazards of high THC levels themselves, and no data currently

exists to suggest the minimal additional exposure to smoke toxins outweighs the hazards due to THC intoxication. Researchers, including CMCR, are looking into ways to have subjects ingest marijuana by methods other than smoking. As such, the smoke toxins issue would be irrelevant under these circumstances.

Prior to 1999, researchers were not charged for marijuana. Since 1999, when HHS established the policy-making marijuana available for medical research, projects that are not funded by the NIH are charged for the marijuana at the cost of production. The price varies depending on the type of marijuana needed by the researcher.

Proposed Testimony of Drug Science Specialist Matthew Strait

Matt Strait will testify about his jobs, experience, training and education while with DEA. He will explain his past and present positions and duties with DEA.

On January 13, 2004, Drug Science Specialist Matthew Strait and Helen Kaupang met with various persons who worked for NIDA. They were Steven Gust, Ph. D., Director of International Operations, Office of Science Policy and Communications, Richard Hawks, Ph. D., Deputy Director, Division of Treatment Research and Development, Timothy Condon, Deputy Director of NIDA, and Kenneth Goodling, Contracting Officer. The purpose of the meeting was for DEA to obtain information from NIDA about the marijuana-drug supply program, the selection of U. Miss. to cultivate and supply marijuana and any information NIDA might have about the quality of marijuana used by researchers.

On September 23, 2004, Mr. Strait met with the (CMCR) researchers and representatives in San Diego, California. The purpose of the meeting was to discuss CMCR researchers' opinions about the potency, quantity and availability of marijuana for research from U. Miss. via NIDA. CMCR currently is the only "non-NIH funded" group in the United States conducting research on humans with marijuana to determine its possible use for HIV, cancer and multiple sclerosis. The following participated in the interviews: Dr. Igor Grant, Dr. J. Hampton Atkinson, Dr. Drew Mattison, Heather Bently, Dr. Thomas Martcotte, Shondra Neumayer and Karen Houpt. The principal investigators (PIs) who participated at the meeting were Dr. Jody Corey-Bloom, Dr. Mark Wallace, Dr. Dennis Israelski (via phone), Hector Vizoso (via phone on behalf of Dr. Donald Abrams), Mr. Mark Traves (via phone for Dr. Dennis Israelski) and Mr. Will Toperoff (via phone for Dr. Ellis).

On September 24, 2003, Mr. Strait interviewed Dr. John Polich of the Scripps Research Institute in San Diego opinions about the potency, quantity and availability of marijuana for research from U. Miss. via NIDA. Dr. Polich is funded by NIH to study the effects of marijuana on the central nervous system in both light and heavy marijuana users.

DEA had the interviewees answer questions on a standardized form to Dr. Igor Grant (representing the CMCR Directorate), Dr. Ronald Ellis (via phone), Dr. Jody-Corey Bloom, Dr. Dennis Israelski (via phone), Dr. Mark Wallace and Dr. John Polich. Dr. Abrams answered the questionnaire via phone on September 29,

2003; this phone interview also was conducted by Mr. Strait. Mr. Strait recorded the answers to the questionnaire, had the interview subjects review, and sign the questionnaires.

Upon completion of the CMCR interviews, DEA participants and CMCR staff visited the Clinical Research Facility at the University of California, San Diego, in LaJolla, California, and the Hillcrest Clinical Research Facility. The latter two locations are where the CMCR PIs conduct their research on human subjects who smoke marijuana. Then the DEA participants visited Hillcrest Pharmacy to discuss the process for ordering, receiving and distributing marijuana cigarettes for approved research.

Dr. Igor Grant gave the DEA participants the following background information about CMCR. Dr. Grant noted that the NIH Workshop on the Medical Utility of Marijuana (1997) and the Institute of Medicine (1999) identified medical conditions that warranted further research for the possible therapeutic marijuana effects on appetite stimulation, neurological and movement disorders, analgesia, nausea and vomiting. In light of these developments, the California State Legislature passed the Medical Marijuana Research Act of 1999. This act resulted in the creation of the CMCR; CMCR's legislative goal was to conduct "... high quality scientific studies intended to ascertain the general medical safety and efficacy of cannabis products and examine alternatives forms of cannabis administration."

In order to qualify to participate in CMCR, researchers must pass review by the CMCR's Scientific Review Board (SRB). If the researcher passes this test, the researcher submits a revised proposal to the Research Advisory Panel of California for review. Simultaneously, the researcher submits his or her protocol to HHS's PHS Committee. PHS then makes a recommendation to NIDA as to whether the researcher's protocol has merit and qualifies for NIDA-grown marijuana on a "cost-reimbursable" basis. The researcher then must make the appropriate revisions to the protocol based upon the CMCR's SRB and PHS/NIDA procedures. Then the researcher submits its proposal to the FDA to obtain an IND designation and submits the proposal to DEA as part of its application to obtain a DEA Schedule I research registration.

All the latter steps must be completed before the researcher is permitted to use marijuana for research. Since 2000, 11 approved clinical trials utilizing smoked marijuana, 3 approved clinical sub-studies on side effects and 4 approved pre-clinical trials in laboratory and animal models have been allowed under all these state and federal procedures. These studies will involve the administration of marijuana to a total of 498 subjects throughout their duration.

The California Medical Marijuana Research Act of 1999 required the CMCR to conduct a three-stage research vision with which the CMCR has been and will continue to comply. The first stage entails the use of smoked marijuana. Because smoked marijuana has unhealthy by-products, stage two entails developing non-smoked delivery systems of marijuana such as sprays, patches,

oral forms and suppositories. Consequently, stage three research will involve the isolation and development of novel molecules, which will systematically activate, modulate or deactivate the body's in-built cannabinoid system.

Because Dr. Craker's application to manufacture (cultivate) marijuana was for the purpose of providing marijuana for research, DEA provided questionnaires to CMCR researchers, which focused on availability, potency and quality of the marijuana used for research. The researchers were informed that candid answers would have no impact on future availability of marijuana that they would receive through NIDA. In addition, the researchers were permitted to review their answers and make any additions or changes as necessary before it was returned to DEA in final form. A summary of these statements as answered by the researchers and Dr. John Polich is provided as follows.

The CMCR researchers noted no instances in which there was a lack of marijuana available for approved research. CMCR directors noted that CMCR maintains close coordination with NIDA. During the two to three week period it takes to process an order, CMCR contacts NIDA and identifies the amount necessary based on enrollment in any of the approved studies. The University of California San Diego (UCSD) pharmacy places the order and submits payment. Upon notification to U. Miss. and NIDA approval, the marijuana is sent by U. Miss. to the UCSD pharmacy. There have been no instances in which NIDA refused to supply marijuana to a researcher that has an approved research protocol.

Visual appearance

Two researchers, Drs. Ellis and Wallace, require high potency marijuana (7-8% THC content). Such products must be hand rolled (as opposed to machine rolled) and degrade quicker than lower potency marijuana. NIDA has been and will continue to be amenable to accommodating for these studies requirements. As such, there is no concern for the future availability of marijuana needed for all CMCR research.

Dr. Polich has received only two marijuana orders in the last five years to complete his research and has no problems with either shipment.

All but one of the researchers has examined the cigarettes obtained from NIDA. They note no difference between the appearance of the actual and placebo cigarettes. Dr. Wallace noted no difference between cigarettes containing different potencies. No researcher noted any physical deformities in the appearance of the cigarettes. Dr. Abrams noted that the cigarettes were nicely rolled.

Plant parts

Dr. Igor Grant visited the U. Miss. marijuana-manufacturing site to view plant material. Based upon his observations, Dr. Grant stated that none of the plant parts in the cigarettes makes them unacceptable for CMCR research. Drs. Israelski and Wallace concurred. Dr. Abrams opined that the U. Miss. marijuana did not necessarily mimic marijuana found on the streets of San Francisco (where his population is from) because the U. Miss. marijuana had some stems and seeds.

Dr. Polich, however, indicated that he had never seen a seed or stem in the U. Miss. marijuana and is very pleased with the product.

Freshness

Drs. Israelski and Wallace never received complaints from their research subjects about the freshness of the marijuana, but Drs. Abrams, Corey-Bloom and Ellis reported that some patients reported a "harshness," which the patients described as irritating their throats and producing a cough. Dr. Ellis said one patient was removed from the study due to these symptoms, and Dr. Abrams reported that four of 50 patients were removed from the research for the same reasons. Dr. Polich noted that three out of 100 plus patients reported that the marijuana was similarly "harsh."

Consistency of potency

NIDA guarantees the cigarette potency will fall within a given range of the target dose. Two CMCR researchers opined that the marijuana product potency was consistent. Dr. Ellis stated that two shipments had variability in THC content and that NIDA had been very responsive. Dr. Abrams noted that midway through one of his studies, NIDA informed him that the marijuana potency of the cigarettes was downgraded from 3.9% to 3.5%. Dr. Grant noted that in-house analysis of THC would begin shortly on samples received from NIDA to ensure content of cigarettes used. Other than Dr. Abrams, all researchers noted that the research quality had not been adversely impacted based upon the quality of the research-grade marijuana.

Potency of marijuana supply

At the time the statements were made, very few of the CMCR researchers had completed their research protocol; none could do more than state that at present the potency was adequate.

The CMCR researchers expressed an interest in exploring a range of concentrations in their patient populations, particularly for cancer patients for whom a higher potency might be potentially more efficacious than a lower potency. Higher potencies would have a perceived benefit in that the patient would inhale less smoke and tar. The perceived risk of such higher potency would be to subject the patients to dependence/tolerability. Another problem with high potency marijuana is that for a naïve patient population there would be susceptibility to paranoia and dysphoria. Dr. Polich requires patients to be monitored for up to five hours after consuming 3.5% THC potency before being released for home (via taxi). Dr. Polich noted he would like to see the medical effects of high potency marijuana on occasional users, but he would be very concerned about paranoia and, as such, would require a heightened in-patient setting.

Other issues

CMCR researchers noted that many potential patients were excluded by CMCR's SRB, but Dr. Corey-Bloom stated that many patients who her research team sought did not want to participate because they would be required to smoke marijuana.

Dr. Israelski was presented with a newspaper article, which stated that one of his patients, Philip Alden, dropped out after developing bronchitis. This patient, according to the article, complained about the quality of the marijuana. Dr. Israelski noted that he did not make any such complaints to the newspaper, and he also noted that often the patient's perception of quality is different from the actual quality.

Mr. Strait interviewed Aron H. Lichtman, Ph.D., Associate Professor of Pharmacology and Toxicology, VCU/MCV. Dr. Lichtman is the primary person who has been involved in certain administrative aspects of obtaining marijuana as well as examining the product and utilizing it for approved animal-type research. Mr. Strait told Dr. Lichtman that DEA had developed a standardized questionnaire specifically to gather information concerning the project on which we are working; Mr. Strait advised Dr. Lichtman that the same questionnaire had been administered previously to other researchers in California and that all information gained would be utilized in-house by DEA. Mr. Strait then submitted the questionnaire to Dr. Lichtman by asking the questions and recording Dr. Lichtman's responses. Both Mr. Strait and Dr. Lichtman noted that many of the questions were not geared toward animal studies with marijuana but rather toward clinical studies. At the end of the interview, Dr. Lichtman reviewed the written responses and acknowledged his agreement with the information noted by initialing and dating the pages. A summary of the main points of the interview responses follows.

Dr. Lichtman has conducted research utilizing marijuana since 1989. He currently conducts only animal studies using mice and occasionally rats. The researchers roll their own cigarettes for the study from bulk plant material obtained thru NIDA/RTI, or they use a pipe. The potency of the plant material is controlled by mixing it with a placebo. The research is approved by NIH; the animal review process is conducted by VCU.

Dr. Lichtman has utilized the following products obtained from NIDA: ditch weed (low potency), placebo (extracted) marijuana, and bulk marijuana (3.5-4% THC). He stated there is a visual difference between placebo material and marijuana containing THC, mostly in the color. The placebo is drier and slightly darker in color; it burns more quickly and is cleaner. The THC content of marijuana is sticky and is dirtier when it burns. He said that the products are kept frozen and in the dark to prevent breakdown; they can last for years. The last bulk material was ordered and received sometime in 1999. The bulk plant material contained some twigs and seed, which were removed prior to conducting the research. The researchers would prefer something of a higher potency, but they requested what NIDA informed them was available at the time the studies commenced, which was 3-4% THC. The researchers have read about the availability of higher potency products available in the UK and also know that higher potency products are seized in law enforcement actions. The researchers would be interested in material containing >6% THC and possibly as high as 10%. A concern of using higher potency material would be the degradation of the

material over time. Dr. Lichtman explained how a researcher learns what marijuana plant material is available through NIDA. Dr. Lichtman stated that NIDA has a listing of what is available in inventory.

Proposed Testimony of PHS representative

The Government will present a witness from the United States Department of Health and Human Services (HHS) to testify about the PHS. He or she will explain the duties of the PHS committee in relation to reviewing and approving protocols for marijuana researchers.

This witness will describe the circumstances that led to the formation of the PHS in 1999. This witness will testify that the PHS was created because there was a need to for peer-review research in order to obtain clear results of marijuana's effects.

NIDA was originally tasked with making determinations as to whether or not protocols for marijuana were eligible to receive domestically cultivated marijuana. NIDA, ultimately, did not undertake this specific task because it was not consistent with its mission.

The witness will testify that the coordinator of the PHS Committee identified various experts to conduct an impartial review of the researchers' studies and assess their protocols for scientific quality and the likelihood that such studies would yield beneficial results. If the PHS approves a researcher's application, the researcher then becomes eligible to receive NIDA/NIH marijuana on a cost-reimbursable basis.

Since the PHS Committee review process commenced in 1999, CMCR has been the single source of externally funded marijuana research protocols. The CMCR's review process has been very effective in the development of high quality scientific protocols related to smoked marijuana. Consequently, CMCR protocols have been routinely approved by the PHS Committee.

After PHS approves the researcher's study, the researcher applies for an IND license from the FDA and obtains the DEA registration for a Schedule I researcher. At this point, the researcher is eligible to ask for and receive marijuana for research.

All orders for marijuana (DEA forms 222) are submitted through NIDA and endorsed to RTI.[2] Shipments are made only after authorization has been received from U. Miss. Non-government sponsored researchers are required to pay a fee per cigarette: $7.50 for active ingredient; $8.00 for placebo.

Proposed Testimony of an RTI representative

This witness will testify about the Bioanalytical Chemistry Center for RTI. He or she will explain the history and the function of the RTI as it relates to the production and dissemination of marijuana for researchers.

The timing of when to produce cigarettes and how much to produce for U.S. research purposes is determined by NIDA after consultation with U. Miss. and RTI. In recent years, the annual needs have averaged approximately one batch of

[2] Dr. ElSohly also will testify about some or all of the information related to RTI as set forth under this part of the proposed testimony of Dr. Eggerston.

cigarettes per year. The starting material for each batch is approximately 74 kg. of 11% moisture marijuana. Based on information supplied by RTI, 74 kg. produces a 60% yield or approximately 65,400 cigarettes each containing approximately 0.6 grams of marijuana. RTI's current inventory is capable of producing approximately 475,000 cigarettes, a number sufficient to provide for current levels of approved researcher's requests for the next seven years. If cultivation of marijuana were to cease immediately, RTI would probably already have enough material on hand for the next two years; the limiting factor, which would prevent the timeline from being longer would be the availability of high potency marijuana. DEA typically allows manufacturers of Schedule I and II controlled substances to maintain a six-month surplus inventory. RTI is equipped to conduct more than a single production run each year.

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 years they have received comments periodically concerning the quality of the marijuana cigarettes, although they have not received any in the recent past. 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." RTI also acknowledged that U. Miss. 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 leaves

are large and long and the machine was equipped to deal with larger plant material. Associates in the tobacco industry assisted RTI and those problems have been resolved. RTI has not received any recent complaints about seeds or stems in their finished products.

In some venues, "quality" is linked with "potency," However, RTI has found that claims on "potency" are sometimes based on very little knowledge. Those who would advocate the "need" to utilize higher potency marijuana must consider medical concerns. Studies have shown that marijuana containing more than 6% THC can strip the lining out of the throat and result in ulcerations.

The ability to develop higher potencies has been progressing. An 8% THC marijuana is currently available and 10% THC could be accessible as well. However, one of the challenges being faced by the NIDA M Project 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.

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.

Diversion Investigator James Place

Diversion Investigator James Place (DI Place) will testify that he is a DEA Diversion Investigator who currently works in such capacity at the DEA Hartford Resident Office. He will testify about his training, duties and experience as a Diversion Investigator.

DI Place will testify that to date the Commonwealth of Massachusetts, Department of Public Health, requires Respondent to submit an application and have such application granted before U. Mass. will be permitted to cultivate marijuana in the manner in which it seeks to do so. Respondent has submitted such an application. Although Massachusetts has not granted the application, Massachusetts will defer to DEA to make the ultimate decision on the U. Mass. application.

The person who would operate the marijuana cultivation project for U. Mass. would be Dr. Craker who is a professor of horticulture as the University of Massachusetts. DI Place will testify that if the application were granted, Dr. Craker asserted that he would attempt to develop and grow a higher quality of marijuana than presently available at U. Miss. and supplied by NIDA. The goal would be to raise the THC content to 12 to 15% THC and to refine the harvesting techniques to produce marijuana with more stem material and less seeds.

Dr. Craker informed DI Place that it was his (Dr. Craker's) opinion that the current marijuana provided by NIDA to researchers was low potency and inferior quality with too many stems and seeds. Dr. Craker also stated that a better quality

marijuana might lead to better research results, and, if not, at least the issue would be put to rest.

Dr. Craker indicated that he would obtain the marijuana seeds from either a domestic or foreign source. *See* answer to bulk manufacturing questions, number 2, Government Exhibit 3.

DOCUMENTARY EVIDENCE

1. Copy of U. Mass. application for DEA registration (3 pages)
2. Copy of resubmitted U. Mass. application for DEA registration (4 pages)
3. Copy of questions pertaining to the application and answers (5 pages)
4. Copy of a Federal Register Notice announcing the U. Mass. application (1 page)
5. Copy of comments and objections submitted by Mahmoud A. Elsohly, Ph. D., of U Miss., in response to the Federal Register Notice announcing the U. Mass. application (3 pages)
6. Copy of U. Miss. Abstract "Screening and Selection of high THC yielding elite clones of a field grown variety (CMCF-02) of *Cannabis Sativa*" (1 page)
7. Copy of U. Miss. Abstract "Vegetative Propagation of *Cannabis Sativa*: An overview from Indoor to Outdoor Cultivation" (1 page)
8. Copy of U. Miss. Abstract "Effect of two different fertilizers on THC and other cannabinoid content, total biomass production and seed production potential in a high yielding variety of *Cannabis Sativa*" (1 page)
9. Copy of an "Order and Assurance Form" for release of marijuana from U. Miss. to approved marijuana researchers (1 page)

10. Copy of "Release and Indemnity Agreement," which requires that researchers who receive U. Miss. marijuana must indemnify U. Miss. and the applicable U.S. government agencies (1 page)

11. CSA facsimiles or DEA registration records of the DEA marijuana registrations for the U. Miss. (unknown pages)

12. Copy of 1999 NIDA contract between NIDA and U. Miss./RTI (unknown pages)

13. Copy of 2004 NIDA contract between NIDA and U. Miss./RTI (unknown pages)

14. Copies of correspondence between the INCB and DEA (4 pages)

15. Copy of a NIDA/NIH "Request for Proposal (RFP) no. N01DA-9-7078" for "Production, Analysis and Distribution of Cannabis and Marijuana Cigarettes," including listed attachments (30 pages)

16. Copy of a report, dated September 23, 2003, of an interview with CMCR representatives (19 pages)

17. Copy of a report, dated September 23, 2003, of an interview with CMCR Ronald Ellis, Ph. D., M.D. (12 pages)

18. Copy of a report, dated September 23, 2003, of an interview with CMCR Jody Corey-Bloom, Ph.D., M.D. (12 pages)

19. Copy of a report, dated September 23, 2003, of an interview with CMCR Dennis Israelski, M.D. (12 pages)

20. Copy of a report, dated September 23, 2003, of an interview with CMCR Mark Wallace, M.D. (12 pages)

21. Copy of a report, dated September 23, 2003, of an interview with CMCR Donald Abrams, M.D. (12 pages)

22. Copy of a report, dated September 23, 2003, of an interview with Scripps Research Institute's Dr. John Polich (12 pages)

23. Copy of an "HHS Fact Sheet," dated May 15, 2002 (4 pages)

24. Copy of *Announcement of the Department of Health and Human Services Guidance on Procedures for the Provision of Marijuana for Medical Research*, National Institute of Health, May 21, 1999 (5 pages)

25. Copy of "Workshop on the Medical Utility of Marijuana," which is the full text of the "NIH Guide: Announcements of the Department of Health and Human Services," dated May 21, 1999 (36 pages)

26. Copy of an RTI flow chart for the production of cigarettes (1 page)

27. Copy of a list of batches of marijuana cigarettes produced at RTI (2 pages)

28. Copy of an interview report for Aron Lichtman, Ph. D. (12 pages)

29. Copy of a letter, dated March 4, 2003, from DEA to Lyle E. Craker, Ph. D. (2 pages)

30. Copy of a letter, dated June 2, 2003, from Lyle E. Craker, Ph. D. to DEA (1 page)

31. Copy of April 1, 2000 testimony before Congressional House Government Reform Committee, Subcommittee on Criminal Justice, Drug Policy, and Human Resources, by NIDA Director Nora D. Volkow (4 pages)

32. Copy of California Health and Safety Code § 11362.9 (2005), the "California Marijuana Research Program" act (5 pages)

33. Copy of *First Medicinal Cannabis Studies Approved by University of California-Based Research Center*, Ascribe Newswire, February 22, 2001 (2 pages)

34. Copy of 42 U.S.C. § 281 (2004)- "Organization of the National Institutes of Health" (5 pages)

35. Copy of 42 U.S.C. § 241 (2004)- "Research and investigations generally" (8 pages)

Respectfully submitted,

Brian Bayly
Senior Attorney
Office of Chief Counsel

Dated: February 28, 2005

CERTIFICATE OF SERVICE

On February 28, 2005, I sent, via Federal Express, postage prepaid, a copy of the foregoing to Lyle E. Craker, Ph. D., University of Massachusetts, Department of Plant and Soil Science, Amherst, Massachusetts 01003, and filed the original and two copies of the foregoing at the DEA Office of Administrative Law Judges by hand delivery.

Brian Bayly