

The Public Interest in the Application
of the University of Massachusetts at Amherst (UMass Amherst) to DEA
for a License to Produce Marijuana for FDA-Approved Research

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EXECUTIVE SUMMARY

An important component of the institutional mission of the National Institute on Drug Abuse (NIDA) is to support scientific research investigating the harmful effects of drugs with abuse potential, such as marijuana, cocaine, heroin, MDMA (Ecstasy), LSD, and many other substances. In furtherance of its mission, NIDA maintains a substantial inventory of these drugs that it provides to scientific researchers with NIDA grants to study the harmful effects of these substances.

NIDA's mission does not include the facilitation of research into the potential beneficial medical uses of these drugs. At present, NIDA is the sole source of the supply of marijuana, but not of any other illegal drug, that can be used in FDA-approved research. As a result of NIDA's restrictions on the supply of marijuana, it is of necessity involved in issues related to providing marijuana to researchers seeking to explore marijuana's beneficial medical uses under an FDA-approved Institutional New Drug (IND) application.

NIDA's restrictions on the supply of marijuana have resulted in problems of access and quality which hinder research into the potential beneficial medical uses of marijuana. NIDA has denied marijuana to two privately-funded, FDA-approved researchers who sought to purchase NIDA marijuana at cost, on the grounds that NIDA didn't like the design of the protocols. Furthermore, NIDA provides lower quality material than some sponsors and researchers would chose to study, thus increasing marijuana's risk profile and making it more difficult to demonstrate a favorable risk/benefit ratio to FDA.

When the federal medical marijuana research process is perceived as politically obstructed, proponents of the medical use of marijuana turn to state ballot initiatives or legislation that bypass FDA evaluation of safety and efficacy and remove state penalties for the medical use of marijuana. Though the US Supreme Court reaffirmed federal jurisdiction over state medical marijuana initiatives and laws, federal authority and credibility are eroded when millions of people or their state representatives vote to override the FDA review process.

The medical use of marijuana should be evaluated through scientific research with a product of the sponsor's and researcher's choice, manufactured by or under contract to the sponsor of the research, with a review process identical to that for other Schedule I drugs.

The public interest would be served by DEA granting the application of University of Massachusetts at Amherst (UMass Amherst) for a license to manufacture marijuana for scientific and medical uses approved by FDA and DEA. When the UMass Amherst facility is licensed and its product is approved by FDA for use in clinical trials, NIDA would not need to be involved with supplying marijuana for research investigating marijuana's potential medical uses.

BACKGROUND

On June 26, 2001, the UMass Amherst Office of Grants and Contract Administration, on behalf of Prof. Lyle Craker, Department of Plant and Soil Sciences, filed with the Massachusetts Department of Public Health an Application for Registration to Manufacture or Distribute Controlled Substances Within the Commonwealth. The UMass Amherst Office also mailed to the Drug Enforcement Administration (DEA) a completed DEA Form 225. These applications were for state and federal licenses to grow marijuana exclusively for Food and Drug Administration (FDA) and DEA-approved uses.

Expenses for equipment and staff for the UMass Amherst production facility will be provided for in the form of a grant from the Multidisciplinary Association for Psychedelic Studies (MAPS), an IRS-approved, Section 501 (c) (3) non-profit research and educational corporation, under the terms of a November 7, 2000 memorandum of understanding between UMass Amherst's Department of Plant and Soil Science and MAPS. The initial production goal for the first year of operation is 25 pounds of high-potency marijuana (12-15% THC). A comprehensive description of the production processes and analytical data about the product will be submitted to the FDA for its review and approval prior to use of the product in FDA-approved research.

MASSACHUSETTS APPLICATION FOR REGISTRATION

On August 9, 2001, inspectors from the Massachusetts Department of Public Health conducted a site visit at UMass Amherst and met with Prof. Craker. Subsequently, the inspectors requested written responses to several questions, which Prof. Craker supplied.

On December 3, 2001, Mr. Michael Mozzer, Assistant, Director for Operations, Division of Food and Drugs, Massachusetts Department of Public Health, spoke by phone with Rick Doblin, Ph.D., MAPS President. Mr. Mozzer informed Dr. Doblin that the Department of Public Health had no objections in principle to the application. However, as a result of his consultation with Ms. Cari Robertson, Group Supervisor, DEA Diversion Control, Boston office, Mr. Mozzer recommended that further evaluation of the security requirements for the facility be postponed until DEA decided whether it would approve in principle the licensure of the facility should all security concerns be appropriately resolved.

CURRENT DRUG ENFORCEMENT ADMINISTRATION POLICY

On November 28, 2001, a press release by University of California's Center for Medicinal Cannabis Research (CMCR) announced that it had received DEA approval to begin two clinical studies on the possible efficacy of cannabis in the treatment of two severe medical disorders, Spasticity in Multiple Sclerosis and Painful HIV Neuropathy. These protocols will use marijuana supplied by NIDA. DEA Administrator Asa Hutchinson was quoted as saying "This announcement is consistent with the DEA position that the question of whether marijuana has any legitimate medical purpose should be determined by sound science and medicine."

On December 5, 2001, Ms. Cari Robertson spoke by phone with Dr. Doblin. She indicated that DEA had questions about whether it was in the public interest to grant the license, primarily because the National Institute on Drug Abuse (NIDA) already contracts with Prof. Mahmoud Elsohly, University of Mississippi, to provide marijuana for FDA-approved research. In response, Dr. Doblin offered to produce a short written analysis for DEA review summarizing why it is in the public interest for DEA and the Massachusetts Department of Public Health to license UMass Amherst to produce marijuana under a grant from MAPS exclusively for scientific and medical purposes that have been approved by the FDA and/or the DEA.

THE RATIONALE FOR THE PUBLIC INTEREST IN GRANTING THE LICENSES

1. MAPS has a Congressionally-sanctioned commercial interest in the development of marijuana as a prescription medicine for AIDS Wasting Syndrome.

On May 25, 1999, FDA's Office of Orphan Products Development approved MAPS' application to have marijuana declared an Orphan Drug for the treatment of AIDS Wasting Syndrome, under a program created by Congress to facilitate the development of drugs for rare diseases. Marijuana's designation as an Orphan Drug for AIDS Wasting Syndrome is currently the only indication for which marijuana has been designated an Orphan Drug. MAPS is considering applying to FDA's Orphan Drug program to have marijuana designated an Orphan Drug for other rare diseases for which marijuana may prove beneficial. MAPS is also considering seeking FDA approval of INDs for research into the use of marijuana for indications that affect too many patients to qualify for Orphan Drug designation.

In addition to its own drug development plans, MAPS intends to supply marijuana produced at UMass Amherst to other approved researchers who request access to its supply, either at cost or for free. Granting a license to the UMass Amherst facility will thus facilitate both MAPS-supported medical marijuana research as well as research by other approved investigators. Once the UMass Amherst facility is licensed and its product is approved by FDA for use in clinical trials, NIDA would not need to be involved at all with supplying marijuana for research investigating marijuana's potential medical uses.

2. MAPS requires a better quality product than NIDA can supply.

MAPS has determined that it needs to conduct research with marijuana of a different variety and potency than is available from NIDA. In order for MAPS to improve the safety profile of its product, MAPS requires marijuana with a THC-content in the 12-15% range, thereby reducing the amount of particulate matter inhaled per unit of THC and improving the risk/benefit ratio of the product. However, NIDA only offers several varieties of marijuana, ranging in potency from 2-7% THC.

MAPS has funded a study evaluating the potency of marijuana used by medical marijuana patients who obtain their supplies from marijuana buyers clubs around the country.¹ The study determined that many patients are already regularly using marijuana with 12% THC or greater. This demonstrates that many patients already use higher potency marijuana than NIDA provides, and that the concern about the possible “behavioral toxicity” of more potent marijuana is not a significant issue for these patients.

The material that NIDA has supplied to the FDA-approved study being conducted by Dr. Dennis Israelski, Department of Public Health, San Mateo County, California, has already proven to be of such low quality that the study has been compromised. One of the few subjects in the study has withdrawn due to throat irritation caused by the NIDA material, in order to resume the use of higher potency marijuana purchased through buyers clubs.²

¹ Gieringer D. Medical Cannabis Potency Testing Project. MAPS Bulletin, 9 (Autumn 1999) 3:20-22. <http://www.maps.org/news-letters/v09n3/09320gie.html>

² Freeling, Nicole Achs. Lone Patient Quits Marijuana Study. Half Moon Bay Review, October 13, 2001. The article reports, “One evening last week, AIDS activist Phillip Alden unpacked some groceries in the kitchen of his stylishly appointed Redwood Shores condominium and prepared for his daily pre-dinner ritual. Alden, a long-time AIDS survivor, pulled a tightly rolled joint of marijuana from a plastic medicine jar, noted it on an index card, and then settled back into his recliner and took a long drag. Seeds in the cigarette sparked and popped. “I know after I take a few hits that within 10 minutes I'm going to be hungry and my nausea is going to go away,” said Alden, who suffers from chronic persistent wasting syndrome, a condition that inhibits the body's ability to absorb nutrients. He says the drug gives him the appetite to keep the pounds on. Last Thursday, however, in a development that could be a serious setback to San Mateo County's groundbreaking study on the medicinal use of pot, Alden's participation came to an abrupt end. A sudden throat inflammation, which he blamed on the poor quality of the pot, left Alden unable to eat and gulping for air. Alden said the marijuana was not as good as the pot he was used to getting from Bay Area cannabis clubs. “The pot was stale and it was full of seeds. When marijuana seeds burn, they smell and taste really bad.” Apparently, the two joints a day that he was required to smoke through the study had aggravated a throat condition. The doctor issued an edict - no more smoking...The marijuana is grown in a federal government laboratory at the University of Mississippi, and then shipped to the San Mateo County Hospital, where it is kept under lock and key. It arrives dried and frozen and is rehydrated the night before it is dispensed to patients. “In terms of the quality of the marijuana, we have to go by what the patients say since we're not trying it ourselves,” Messenger [an assistant to program director Dr. Dennis Israelski] said. “We know the level of THC is lower in this federal-provided marijuana, but unfortunately we don't have any control over that. We have to use whatever we're given by the federal government for this study.” The joints are rolled in tobacco-company cigarette paper, rather than traditional rolling papers. Alden said that besides the poor quality of the pot he believed the cigarette paper was harsher on his throat...During the study, Alden would smoke a marijuana cigarette in the evening before dinner to stimulate his appetite and another before bed to calm his stomach. Once his throat condition clears, Alden says he will go back to treating himself at the cannabis clubs. “It works. I have no doubt about that,” he said.”

MAPS further seeks to improve the safety profile of its product by following a recommendation of the Institute of Medicine (IOM), which conducted a study of the medical use of marijuana that was funded by the Office of National Drug Control Policy (ONDCP).³ The IOM report recommended the development of non-smoking delivery systems for the medical use of marijuana. MAPS intends to use high-potency marijuana in conjunction with a vaporizer device that heats marijuana to temperatures just short of combustion, resulting in a vapor that is much like steam. MAPS has conducted research that has demonstrated that marijuana vapor is largely absent of toxic combustion products that result from the burning of marijuana, or any other plant material.⁴ Due to the lower potency of NIDA's supply of marijuana, its product will not work as well with vaporizers as would marijuana produced by UMass Amherst, and would not produce an accurate assessment of the risks and benefits of the product that MAPS seeks to study.

3. Marijuana supplied by NIDA for research is not available for marketing under an approved New Drug Application (NDA).

Data in a New Drug Application (NDA) submitted to FDA must come from clinical trials that have been conducted with the identical product for which approval for marketing is requested. However, there is no guarantee that marijuana provided by NIDA for research would be available for commercial use. NIDA-supplied marijuana is therefore inadequate for use in a privately-funded drug development plan. Only an independent supply that is guaranteed to be available for research and possible prescription use, such as would be produced at UMass Amherst, would be sufficient.

NIDA has contracted with Prof. Elsohly to produce marijuana for research purposes, not for sale of marijuana as a prescription medicine. MAPS has previously asked Dr. Elsohly to grow marijuana under contract to MAPS for both research and possible prescription use. Dr. Elsohly declined out of concern that such a contract might be negatively perceived by NIDA and cause him difficulty in renewing his grant to produce marijuana for NIDA. No rational pharmaceutical company would invest millions of dollars in Phase III clinical trials of a drug that it cannot be certain it could produce for commercial sale should safety and efficacy be demonstrated to the satisfaction of the FDA.

4. NIDA's requirement of approval adds an extra layer of governmental review of privately-funded FDA- and DEA-approved protocols which is not required for any other Schedule I drug and which slows and sometimes prevents marijuana research .

Prior to May 21, 1999, NIDA insisted that it review and approve all privately-funded, FDA-approved protocols even when researchers sought to purchase, rather than be given, supplies of NIDA's marijuana. On one occasion, NIDA refused to permit researchers to

³ Joy J, Watson S, Benson J (eds.): Marijuana and Medicine: Assessing the Science Base. Washington, DC: Institute of Medicine, National Academy Press, 1999. <http://stills.nap.edu/books/0309071550/html>

⁴ Gieringer, D. MAPS/NORML Study Shows Vaporizers Reduce Toxins in Marijuana Smoke. MAPS Bulletin, 11 (Spring, 2001) 1: 20-21. <http://www.maps.org/news-letters/v11n1/11120gie.html>

purchase marijuana for an FDA-approved protocol.⁵ NIDA objected to the protocol design, even though the protocol had already been thoroughly reviewed and approved by FDA.

On May 21, 1999, NIH issued new guidelines for obtaining access to NIDA's supply of marijuana.⁶ Privately-funded researchers were formally permitted to purchase marijuana at cost from NIDA⁷ but were required by NIH to undergo an extra review process to be conducted by the Public Health Service (PHS).⁸ The PHS review process is in addition to required approvals from FDA and DEA and is not required for privately-funded FDA and DEA-approved research with any other Schedule I drug because NIDA is the sole source of supply only of marijuana. As a result, privately-funded researchers with FDA and DEA approval can obtain supplies of all other Schedule I drugs from non-NIDA sources and are therefore not required to obtain NIDA or PHS approval.⁹ On one occasion, PHS rejected an FDA-approved medical marijuana protocol, again over concerns about protocol design, despite the fact that no public money was going to be spent on the clinical trial and the marijuana was going to be purchased at cost from NIDA.¹⁰

NIH's requirement that the PHS also review protocols approved by FDA and DEA went against the recommendations made by an NIH-selected Ad Hoc Group of Experts, convened by NIH for its February 19-20, 1997 conference on the Medical Utility of Marijuana. The Ad Hoc Group of Experts were asked by NIH to review and summarize the existing research literature and also to accept and consider public comment. The Ad Hoc Group of Experts recommended that, "Whether or not the NIH is the primary source of grant support for a proposed bona fide clinical research study, if that study meets U.S.

⁵ Dr. Donald Abrams' IND #43,542, A Prospective, Randomized Pilot Study of High, Medium or Low THC-content Smoked Marijuana on Weight Loss in Persons with HIV-related Wasting Syndrome versus Dronabinol. <http://www.maps.org/mmj/v6proto.html>

⁶ Guidance On Procedures for the Provision of Marijuana for Medical Research. Department of Health and Human Services. May 21, 1999. <http://www.mpp.org/hhsguide.html>

⁷ "To facilitate research on the potential medical uses of cannabinoids, HHS has determined that it will make research-grade marijuana available on a cost-reimbursable basis, subject to the priorities and conditions described in section III, below." Ibid., Section II. Availability of Marijuana for Research Purposes.

⁸ "After submission, the scientific merits of each protocol will be evaluated through a Public Health Service interdisciplinary review process...In addition, researchers who propose to conduct investigations in humans must be able to fulfill the Food and Drug Administration's investigational new drug (IND) requirements and must obtain a valid registration from the Drug Enforcement Administration (DEA) for research with Schedule I drugs." Ibid., Section III. Elements for Considering Proposed Studies.

⁹ MAPS is sponsoring FDA-approved research with MDMA (Dr. Mithoefer's IND #63,384. A Human Pilot Study of the Safety and Efficacy of 3,4-Methylenedioxymethamphetamine (MDMA) -assisted Psychotherapy in the Treatment of Chronic PTSD, <http://www.maps.org/research/mdma/protocol/index.html>), and has helped fund FDA-approved research with psilocybin (Dr. Moreno's IND # 56,530, Effects of Psilocybin in Obsessive-Compulsive Disorder, <http://www.maps.org/news/1099news.html>). In both cases, MAPS was able to contract with DEA-licensed chemists to manufacture the research material to a level of purity and stability that met FDA standards. NIDA was not involved with either study and no extra protocol review by NIDA and the PHS was required.

¹⁰ Dr. Ethan Russo's IND #58,177, Cannabis in Acute Migraine Treatment. <http://www.maps.org/mmj/mjrusso.html>.

regulatory standards (U.S. Food and Drug Administration (FDA) protocol approval and Drug Enforcement Administration (DEA) controlled substances registration) the study should receive marijuana and/or matching placebos supplied by the National Institute on Drug Abuse (NIDA). In this way, a new body of studies may emerge to test the various hypotheses concerning marijuana.”¹¹

NIH’s requirement that the PHS review privately-funded FDA and DEA-approved protocols also went against ONDCP policy as stated in a July 5, 1994 letter by Director Dr. Lee Brown to DEA Administrator Tom Constantine. Dr. Brown was responding to a letter he had received from FDA Commissioner Dr. David Kessler, who was concerned about DEA objections to the design of Dr. Donald Abrams’ FDA-approved medical marijuana protocol. Dr. Brown wrote, “I have asked my deputy, Mr. Fred Garcia, to inform FDA (also enclosed) that at this time we do not wish a departure from established policy, which is to treat research on the therapeutic use of marijuana the same as research on any other drug of abuse potential. Nor do we wish to encourage a blurring of well-established responsibilities and working relationships. I am confident that I can count on your assistance in maintaining established policy in this area.”¹² Though Dr. Brown stated that ONDCP policy was to treat research on the therapeutic use of marijuana the same as research on any other drug of abuse potential, NIDA’s restrictions on the supply of marijuana that can be used in FDA-approved research and the extra layer of PHS review of privately-funded FDA-approved protocols are unique to marijuana.

CONCLUSION

When the federal medical marijuana research process is perceived as politically obstructed, proponents of the medical use of marijuana turn to state ballot initiatives or legislative actions that bypass FDA evaluation of safety and efficacy and remove state penalties for the medical use of marijuana. Though the US Supreme Court has reaffirmed federal jurisdiction over state medical marijuana initiatives, federal authority and credibility are eroded when millions of people or their elected representatives vote to override the FDA drug review process.

As long as NIDA retains its monopoly on supply, some researchers and sponsors of research are forced to decide whether to conduct studies with a product whose quality they believe is sub-optimal, increasing health risks and compromising the use of the non-smoking delivery device known as the vaporizer, thereby biasing the research results. Sponsors will have no other option than to choose whether or not to conduct a drug development plan with a material that may not even be available for prescription use, thus increasing the economic risks of proceeding with any research. As long as the NIH guidelines require PHS review, the approval process for medical marijuana research will be more onerous and arbitrary than research with other Schedule I drugs. As long as

¹¹ Workshop on the Medical Utility of Marijuana: Report to the Director, National Institutes of Health. National Institutes of Health, February 19-21, 1997.

<http://www.nih.gov/news/medmarijuana/MedicalMarijuana.htm>

¹² Brown L. Director, Office of National Drug Control Policy. Letter to DEA Administrator Tom Constantine. July 5, 1994. This letter was obtained by FOIA request.

NIDA is the sole source of supply, the FDA process will rightly be perceived by the public as obstructed, further fueling efforts by states to circumvent federal authority over the medical uses of marijuana through ballot initiatives or state legislation.

It is therefore in the public interest for DEA and the Massachusetts Department of Public Health to license the UMass Amherst production facility, with whatever security systems and procedures are required to eliminate diversion. Approval for research will still be required by FDA, DEA and local Institutional Review Boards (IRBs) before any clinical trials of medical marijuana can be conducted. The medical use of marijuana should be decided through scientific research with a commercial product of the sponsor's choice, manufactured by or under contract to the sponsor, with a review process identical to that for other Schedule 1 drugs.