UNITED STATES DEPARTMENT OF JUSTICE
DRUG ENFORCEMENT ADMINISTRATION

In the Matter of	)	
	)	
	)	Docket No. 05-16
LYLE E. CRAKER, PH.D.	)	
	)	

RESPONDENT'S OPPOSITION TO THE DEA'S MOTION IN LIMINE TO EXCLUDE SOME OF RESPONDENT'S PROPOSED TESTIMONY AND EXHIBITS

Respondent opposes the Government's Motion in Limine to Exclude Respondent's Proposed Testimony and Listed Exhibits Pursuant to 5 U.S.C. § 556(d) and 21 C.F.R. § 1316.59(a), (hereinafter "Gov't Motion"). Respondent's proposed witnesses and exhibits are relevant to the issues before the court and will be of substantial aid to the decision maker.

As a result, the court has a duty to hear the evidence. Relevant evidence is defined as that which has "any tendency to make the existence of any fact that is of consequence to the determination of the action more probable or less probable than it would be without the evidence." Fed. R. Evid. 401. The standard of relevance is thus a liberal one. *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 587 (1993). This is especially so in the context of an administrative hearing, where an ALJ has a duty to err on the side of inclusion when considering the relevance of evidence. *Underwood v. Elkay Mining*, 105 F.3d 946, 951 (4th Cir. 1997). Indeed, it is an error to exclude evidence even if it is of reduced relevance. *See Brown v. Sierra Nevada Memorial Minors Hosp.*, 849 F.2d 1186, 1190 (9th Cir. 1988).

As we will show, Respondent's witnesses and exhibits are clearly relevant to the factual and legal issues to be considered at the hearing. DEA erroneously and without explanation reduces the six statutory factors which outline the public interest to the single factual issue of

whether the sole current manufacturer satisfies part of the first statutory factor. This mischaracterization of the issues before the court cannot justify the exclusion of relevant evidence.

The Issues Relevant to the Hearing

The issue to be decided at the hearing is whether granting Respondent's application to be a manufacturer of marijuana for research would be in the public interest, as defined by 21 U.S.C. § 823(a). Prehearing Ruling at 1. Respondent's witnesses and exhibits are all relevant to factors set forth in this statute, and therefore to this issue.

21 U.S.C. § 823(a) provides that the Attorney General "*shall* register an applicant" if such registration is consistent with the public interest and with U.S. treaty obligations. (emphasis added). Thus, the ultimate issue is whether the license will further the public interest. To determine that public interest, "the following factors *shall* be considered":

> (1) maintenance of effective controls against diversion of particular controlled substances and any controlled substance in schedule I or II compounded therefrom into other than legitimate medical, scientific, research, or industrial channels, by limiting the importation and bulk manufacture of such controlled substances to a number of establishments which can produce an adequate and uninterrupted supply of these substances under adequately competitive conditions for legitimate medical, scientific, research, and industrial purposes;
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> (2) compliance with applicable State and local law;
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> (3) promotion of technical advances in the art of manufacturing these substances and the development of new substances;
>
> (4) prior conviction record of applicant under Federal and State laws relating to the manufacture, distribution, or dispensing of such substances;

> (5) past experience in the manufacture of controlled substances, and the existence in the establishment of effective control against diversion; and
>
> (6) such other factors as may be relevant to and consistent with the public health and safety.

21 U.S.C. § 823(a) (emphasis added). If Respondent's witnesses and exhibits are relevant to any of the five specific factors, or to *any other issue* relevant to public health and safety, as provided in factor (6), they are admissible. 5 U.S.C. § 556(d); 21 C.F.R. § 1316.59(a).

The DEA seeks to exclude four witnesses and various exhibits from Respondent's case. It argues that the evidence is irrelevant because, in DEA's view, the "primary" issue at the hearing is whether "the current cultivator of research marijuana, the University of Mississippi, produces an adequate quantity or acceptable quality of marijuana for research purposes, and whether another cultivator of marijuana is needed to supply marijuana for scientific investigations and new drug products."[1] Gov't Motion at 3. (Interestingly, DEA fails to mention the statutory concern for "adequately competitive conditions.") DEA argues that any witness or exhibit not relevant to this specific factual issue should be excluded.

DEA's treatment of this lone issue as a "threshold factor" is inconsistent with the statute. As just noted, Section 823(a) articulates five specific factors (without any indication that any of them are "threshold" factors), and mandates consideration of any other factors relevant to public health and safety. 21 U.S.C. § 823(a). It does not even suggest that factor (1) should be considered differently than the others. To the contrary, the statute mandates that in determining the public interest the agency "shall" consider all

[1] Remarkably, the DEA says this characterization of the issue is *Respondent's*. See Gov't Motion in Limine at 3 (noting the "primary factual issue, however, *as framed by Respondents"*). It cites does so without any citation to any source, however, and for a very good reason, since Respondent has not, and does not now, frame the "primary" issue for the hearing in that way.

those factors. *Id.* DEA certainly may not ignore five-sixths of the statutory language. *Id.* In addition, the statutory factors are interrelated, not wholly independent. For example, even if the current manufacturer had, to date, produced an "adequate" supply under "adequately competitive conditions," a proposal for bulk manufacturing cannabis with different characteristics suitable for a different delivery system would certainly justify the conclusion that the existing supply is *inadequate* to support a potential technological advancement. Thus, factor (3), relating to those advancements, would affect consideration of factor (1). As this example shows, DEA's suggestion that no evidence can be relevant unless it directly relates to the factual issue DEA posits is clearly misplaced.[2]

DEA also appears to have invented an evidentiary presumption that the status quo at the time of a license application to manufacture marijuana for research meets the public interest test, and that all of Respondent's evidence must show that it does not. Thus, DEA repeatedly challenges evidence on the grounds that it does not, in DEA's jaundiced view, tend to prove that the University of Mississippi does not provide and adequate and uninterrupted supply. Gov't Motion at 4. This presumption is found nowhere in the statute. 21 U.S.C. 823(a). To the contrary, the law requires the agency to examine whether, in light of the application, the public interest is best served by granting the license, considering the five specific factors and any other factor relevant to public health and safety. DEA is required to consider many factors in addition to whether there is an adequate supply under competitive conditions, such as, among other things, whether Dr. Craker's application would promote technical advances in the art of manufacturing marijuana, promote development of new substances, increase competition from

[2] Nor is it likely that DEA really believes this assertion since it offers much testimony and exhibits that are not relevant to that factor, such as Ex. 37 - 43, 48 - 52, 8l - 82, among others.

none to some so as to come closer to the statutorily-required "adequately competitive conditions" and serve the public health and safety. *Id*. Thus, DEA's attempt to narrowly constrict the evidence that is relevant should fail.

Respondent's Exhibits

The Articles Concerning Past Research on Medical Marijuana Are Relevant To Statutory Factors (1), (3), and (6).

The government proposes to exclude several articles listed as exhibits by Respondent because they "concern past scientific research devoted exclusively to the potential virtues and risk of using marijuana as a medicine." Gov't Motion at 6. First, the government suggests that such research can only be related to factor (3), and then concludes that because past research "has no relevance to the success of Respondent's future endeavors," *id.*, the articles must be excluded as irrelevant. But nothing in the statute requires that Respondent's evidence prove that he will be "successful" in order to be relevant to whether a license will "promote technological advancement." Indeed, technological advancement is often based on earlier failures that point the way to success. Second, the government again repeats that the articles have no relevance to whether the current supply is adequate, and urges exclusion on that ground. But this argument must fail as well, because the articles are relevant to factor (1) as well as to factors (3) and (6) of the statute.

As a category, evidence of existing scientific research on the therapeutic benefits and risks of marijuana as a medicine is certainly relevant to whether the research for which Dr. Craker proposes to cultivate marijuana constitutes "legitimate scientific, medical, [or] research purposes." 21 U.S.C. 823(a)(1). Because it is Respondent's burden to show that its license will

further the public interest by avoiding diversion into "other than legitimate medical, scientific, research, or industrial channels" under factor (1), Respondent must be able to demonstrate that the license he seeks will be used to facilitate legitimate research. It would be strange if Respondent were not allowed to show that the legitimate research it seeks to further is based on, and flows from, such past legitimate medical, scientific research. Indeed, without introducing such evidence, Respondent would be left open to a DEA claim that the research for which it seeks to grow cannabis is not legitimate because he introduced no evidence suggesting that marijuana has any therapeutic benefits that would justify such research.

As a group, these articles also are relevant to the public health need for further medical, scientific, and research purposes (which Respondent contends this license will further), and for further product development to minimize the risks involved with smoked medical marijuana (which Respondent also contends this license will further since one goal is to develop a product that can be used in a vaporizer, a non-smoked delivery system). Thus, they are relevant to factors (3) and (6), which require the DEA to consider whether the license will tend to promote advances as well as "such other factors as may be relevant to and consistent with the public health and safety."

Specifically, *Basic Mechanisms of Cannabinoid-Induced Analgesia* by William J. Martin concludes that cannabis may be a beneficial pain medication if undesirable side effects could be reduced. This article demonstrates that legitimate medical, scientific, and research purposes exist to justify cultivating marijuana despite concerns about diversion, and thus is relevant to factor (1). It also is relevant to the public health and safety, since the public would benefit from an additional pain reliever, and since non-smoked delivery systems would alleviate some of those side effects. Thus, it is relevant to factor (6). It is also relevant to Respondent's position

that cultivating marijuana with varying proportions of THC and cannabinoids may increase the beneficial effects and decrease the undesirable effects, thus promoting technological advances in the art of manufacturing cannabis as medicine, as set forth in factor (3). Given that Respondent contends that NIDA's marijuana is of poor quality and causes greater health risks than a higher quality marijuana would, the article is also relevant to proving that NIDA's facility does not provide an adequate product for legitimate research considered in factor (1) and that it endangers the public health and safety considered in factor (6).

Marijuana as Antiemetic Medicine: A Survey of Oncologists' Experiences and Attitudes by R.E. Doblin and M. Kleiman, a survey of members of the American Society of Clinical Oncology, concludes that a significant minority of physicians have already recommended to at least one patient that they try *smoked* marijuana as a treatment for nausea associated with cancer chemotherapy. The article is therefore relevant to (a) establishing a public health need for marijuana as medicine (factor 6); (b) confirming that Dr. Craker's proposed license for marijuana to be used in FDA-approved research is for legitimate medical, scientific, or research purposes (factor 1); and (c) establishing that technological advances in marijuana as medicine over the pill form will serve the public health (factors 3 and 6) since those with nausea are less likely to keep a pill down.

Inhalation Marijuana as an Antiemetic for Cancer Chemotherapy by V. Vinciguerra, T. Moore, and E. Brennan found that evidence from clinical research with cancer chemotherapy patients neither discredited nor conclusively affirmed the benefits of marijuana as an antiemetic agent and suggested that further research would provide additional and necessary information. This article also reported evidence demonstrating that for some patients, smoked marijuana was more effective than the oral THC pill, Marinol. This article therefore is relevant to whether there

is a need for further legitimate research for which DEA must ensure there is an adequate supply under factor (1), and to whether there is a public health need for technological developments in the delivery system (as Dr. Craker's research sponsors propose to develop and test) as set forth in factors (3) and (6).

Chronic Cannabis Use in the Compassionate Investigational New Drug Program: An Examination of Benefits and Adverse Affects of Legal Clinical Cannabis by E. Russo, et. al. reports on medical evaluations of four of the seven patients who have legally received and used medical marijuana from NIDA for decades. NIDA has never evaluated or studied the effect of marijuana on these patients. Dr. Russo's study concluded that even crude, low-grade marijuana can provide effective relief of pain, muscle spasms and intraocular pressure elevations. Dr. Russo also reported on complaints about the quality of NIDA marijuana from these patients and concluded that "a paramount issue affecting the compassionate IND patients revolves around cannabis quality." Dr. Russo also recommended that "Improvements in a clinical cannabis program would include a ready and consistent supply of sterilized, potent, organically grown unfertilized female flowering top material, thoroughly cleaned of extraneous inert fibrous matter." Dr. Russo also cites a 1989 paper that reviewed the quality of NIDA marijuana and reported that "test subjects in their study of NIDA Cannabis reported . . . that the marijuana is inferior in sensory qualities (taste, harshness) than the marijuana that they smoked outside the laboratory. Some have stated that it was the worst marijuana they had ever sampled, or that it tasted 'chemically treated.'" *Id.*at 48. This article is therefore directly relevant to whether (a) NIDA's current manufacturer provides an adequate product for legitimate research and development of marijuana into a healthy and safe medicine, as considered by factors (1) and (6),

and (b) there is a public health need for technological developments in the delivery system (as Dr. Craker's research sponsors propose to develop and test) as set forth in factors (3) and (6).[3]

Finally, *Marijuana Use and Its Association with Adherence to Antiviral Therapy Among HIV-infected Persons with Moderate to Severe Nausea* by B.C. De Jong, et. al. investigated a subgroup of HIV patients who were better able to adhere to their prescription drug regiment because of smoking marijuana, and *Short-Term Effects of Cannabinoids in Patients with HIV-1 Infection* by D. Abrams, et. al. concluded that neither orally ingested nor smoked marijuana had harmful effects on HIV patients' immune system, but that the results need to be confirmed in larger and longer trials. These studies concluded that more research is needed. The articles thus are relevant to show that legitimate research purposes exist for marijuana, thus requiring the DEA to ensure an adequate and uninterrupted supply under adequately competitive conditions, as set forth in factor (1) and raise the public health needs of those thousands of persons who suffer from HIV/AIDS, and who may be without other options, as set forth in factor (6).

The government also argues that these studies are unduly repetitious, without saying what they repeat. The differing studies, however, show the various medical uses of marijuana as well as the various groups of patients who have benefited or who might benefit from that use. Because of all those different uses, these articles each uniquely contribute to showing the public health need for an adequate supply of research marijuana that will allow further testing and product development of what may be different products that respond to these various problems differently. (Factor 6). And, because Respondent contends that NIDA's existing facility has provided marijuana of lower potency that is generally desired by medical marijuana patients and

[3] Despite this article's specific examination of the use of marijuana from NIDA's facility in testing for medical benefits, the government inexplicably argues that this article is not relevant to factor (1) in the statute.

by some potential sponsors of research, the articles are not repetitious, but are relevant to whether the current manufacturing regime of one cultivator who can grow only according to contract with NIDA provides for sufficient market competition to adequately supply researchers under adequately competitive conditions, as set forth in factor (1).

The Testimony of Angel Raich, and Valerie Coral Is Relevant to Factors (1) and (6).

The government also seeks to exclude the testimony of Respondent's witnesses Angel Raich and Valerie Coral, arguing again that the testimony is not relevant to what DEA views as the threshold issue. Gov't Motion at 8. The testimony of both Angel Raich and Valerie Coral is relevant to statutory factors (1) and (6). Their testimony will provide the ALJ with significant direct evidence of the medical benefits of marijuana, and is relevant to the fact that (a) Dr. Craker's proposed manufacture for FDA-approved research is for legitimate medical, scientific, and research use (factor 1); and (b) the public health need—*expressed directly by members of the public*—for marijuana as a medicine (factor 6). Respondent contends that the needs of patients like these have not been met, and that Dr. Craker's license is in the public interest because it is a necessary prerequisite to a drug developer's ability to privately develop marijuana as FDA-approved medicine.[4]

[4] DEA dismisses the direct testimony of patients whose doctors have told them to use medical marijuana as "anecdotal" and therefore irrelevant. Gov't Br. at 8. Of course anecdotal testimony is not irrelevant, if the anecdotes tend to make the establishment of a fact more likely than it would be without it, as this direct testimony would surely do. DEA also suggests that the testimony should be excluded because "future research" necessary to make a pharmaceutical concern more interested in developing a marijuana product is "highly speculative." *Id.* But whether future research would, *in fact*, result in a new marijuana drug is not at issue here. Respondent need only show that granting the license furthers the public interest because it would "promote"---not guarantee---technological advances and new product development. If the standard were otherwise, no one could ever obtain a license without showing that they could already do what they need the license to accomplish. The statute requires no such showing.

Raich and Coral's testimony also show the difficulty and danger that members of the public face if they are forced to produce and obtain their necessary medicine illegally, instead of being able to obtain it like any other medication. Thus, their testimony is relevant to the public health and safety, which would be improved by a source of research marijuana suitable for private development into medicine (factor 6). They can both testify as to the legal protections they have sought for use of marijuana when those protections were afforded under state laws, and they can state that those cases resulted in a decision that essentially makes the conduct of FDA-approved research the only remaining viable vehicle for patients to obtain the medical benefits of marijuana in a manner that is legal under federal law. Thus, this testimony is highly relevant to the public health and safety, since Respondent contends that the public health and safety would be improved if there were a supply of research marijuana adequate to enable its development into a prescription medicine.

Testimony of Dr. Irwin Martin

Although Dr. Irwin Martin's testimony is entirely different from any of the other testimony the government seeks to exclude, the government simply maintains the same notion that the testimony is somehow not relevant to whether the current supply is adequate, and it is therefore not admissible. The government's position is entirely wrong, as Dr. Martin's testimony is directly relevant to factors (1), (3), and (6). Dr. Martin's testimony

Dr. Martin, an expert in new drug development, will testify that for a rational pharmaceutical company or other sponsor to decide to invest in new drug development (here, of marijuana), one of the prerequisites is that it can ensure an adequate and uninterrupted supply, under adequately competitive circumstances, of the ingredients of the medicine (in this case,

marijuana of the strain and composition best suited, based on the research, to accomplish the objective of the medicine) that could be guaranteed to be available as a prescription medicine should the FDA decide that research justified its approval. He will also testify that no rational new drug developer would embark on such an attempt were it not able to control the quality and makeup, as well as the cost, of the plant critical to the medicine it plans to develop.

Respondent contends the current manufacturer, under contract with NIDA, has not, and cannot, provide such an adequate and uninterrupted supply under adequately competitive circumstances of the particular product best suited to a private drug sponsor's needs, because (1) it may take some research with various strains of marijuana to determine which product is best suited; (2) such private drug sponsors would have to rely on the good graces of the NIDA grower to grow the products it requires; and (3) a private drug sponsor would have no ability to control cost with a NIDA grower, since there is no competition with that single grower to encourage it to keep its costs down. As Dr. Martin's testimony will show, without a licensed manufacturer who has *agreed* to grow various products to conduct that research, to respond to the new drug sponsors requests for changes in product formulation and to meet the conditions necessary for FDA approval, a new drug developer cannot even take the first steps.

Therefore, Dr. Martin's testimony is highly relevant to factor (1) because it directly addresses whether a rational new drug sponsor funding research and development in the area of marijuana as medicine would fund that research without the license that allows their cultivator to grow the critical component of the new drug. Further, when the statute requires that adequate and uninterrupted supplies of marijuana be available for legitimate medical, scientific, and research "under *adequately competitive conditions*," it is plainly referring to market competition which has long been the way that medicines are created and improved in this country. Since

there is now but a single cultivator, there is *no* competition as far as researchers or drug sponsors are concerned that encourages the usual market improvements in both price and quality. Dr. Martin's testimony is also relevant to factor (3) because, as Dr. Martin will testify, a company developing a new drug (in this case, marijuana as medicine) must, as a matter of economics, be free to choose the formulation of the product, as well as how the product will be delivered. Without the ability to control the formulation of the product, a company would not invest the significant amounts of money needed to develop the new product. Thus, Dr. Martin's testimony is relevant to whether the license will help promote technical advances and the development of new substances. And, because Respondent contends that developing marijuana as medicine would advance public health and safety, Dr. Martin's testimony is also relevant to factor (6) since it demonstrates what a new drug developer needs to further the public interest.

Testimony of Lester Grinspoon

Finally, the government seeks to exclude the testimony and book of Dr. Lester Grinspoon because of its "anecdotal" nature. DEA argues that because it found anecdotal evidence less persuasive than empirical studies in a previous hearing regarding rescheduling marijuana, this evidence should therefore be wholly excluded in this hearing. DEA's argument is inapposite. The *persuasiveness* of the evidence in another hearing addressing an entirely different issue has no bearing on whether it is *relevant* for this hearing. Grinspoon's testimony and book is relevant to factor (1) because it demonstrates a need for more conclusive empirical research for which DEA must ensure there is an adequate supply of marijuana. 21 U.S.C. § 823(a). Moreover, although left out of the government's description of his testimony, Grinspoon will also testify about results from controlled clinical studies that bear on the questions of marijuana's potential

medical uses. Dr. Grinspoon will also testify as to the long history of these efforts (which he helped initiate over 30 years ago) to conduct research into the medical uses of marijuana, and about how supply for such research has been extraordinarily difficult to obtain. Thus, his testimony is relevant to factor (1).

Conclusion

Based upon the foregoing, Respondent opposes the Government's Motion In Limine to Exclude Respondent's Proposed Testimony and Listed Exhibits Pursuant to 5 U.S.C. § 556(d) and 21 C.F.R. § 1316.59(a). Because the propose testimony and exhibits are relevant to a the statutorily-prescribed factual and legal issues before the ALJ, the ALJ should deny the motion.

Respectfully submitted,

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Dated: August 8, 2005

CERTIFICATE OF SERVICE

I hereby certify that on August 8, 2005, I caused a copy of the foregoing Respondent's Opposition to the Government's Motion in Limine to be served on the following by facsimile transmission:

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