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March 19, 2007

RE: Assembly Bill 259

URGENT (Committee on Public Safety hearing scheduled for March 27, 2007)

Dear Honorable Assembly Member:

This letter summarizes the important medicinal properties of *Salvia divinorum* and its primary active constituent salvinorin A. It also puts forth several objections to Assembly Bill 259, which inappropriately seeks to make this medicinal herb a Schedule I controlled substance.

As a pharmacognosist who has devoted the last 15 years to the scientific study of this herb, I believe that I am particularly qualified to speak on this issue. I was the first person to investigate the human pharmacology of salvinorin A and to clearly identify this compound as the psychoactive principle of *Salvia divinorum*. My findings have been published in several peer-reviewed scientific journals. These include a paper that was published in *Proceedings of the National Academy of Sciences* (PNAS), in which my research group identified the neurological mechanism of salvinorin A's action. That finding is of particular significance because it provides solid evidence for the medicinal value of this compound. I am currently working in collaboration with several other scientists to further investigate the medicinal potential of salvinorin A and closely related compounds. My collaborators include Dr. Bryan Roth (Project Director of the National Institute for Mental Health Psychoactive Drug Screening Program), Dr. Thomas Munro (pharmaceutical chemist at McLean Hospital Psychiatric Research Center, MA), Dr. Lee-Yuan Liu-Chen (professor of pharmacology at Temple University School of Medicine), and Dr. Jordan Zjawiony (Pharmacognosy and Research Professor in the Research Institute of Pharmaceutical Sciences, University of Mississippi). In addition to these endeavors, I am presently completing work on a comprehensive academically oriented book about *Salvia divinorum*.

Medicinal properties

There are approximately one thousand species of *Salvia* worldwide. *Salvia divinorum* is just one of the many species that are recognized for their useful medicinal properties. The common name for salvia is *sage*. Most people are familiar with the common culinary sage, *Salvia officinalis*, which in addition to its usefulness as a flavoring agent, is also used for its medicinal properties. The genus name *Salvia* is derived from the Latin *salvare*, meaning "to heal" or "to save." The words *salvation* and *savior* also come from this same root.

Salvia divinorum is endemic to the Mazatec region of central Mexico, where it has a long history of medicinal use. The Mazatec people use this herb for its psychoactive properties and as an effective treatment for arthritis, headache, and eliminatory complaints. The validity of each of these different applications is well supported by recent pharmacological findings.

Salvinorin A is a uniquely potent and highly selective kappa-opioid receptor agonist, and as such, it has tremendous potential for the development of a wide variety of valuable medications. The most promising of these include safe non-addictive analgesics, antidepressants, short-acting anesthetics that do

not depress respiration, and drugs to treat disorders characterized by alterations in perception, including schizophrenia, Alzheimer's disease, and bipolar disorder.

Kappa-opioid receptor agonists are of particular interest to pharmacologists because they provide effective pain medications that are not habit forming and do not produce dependence. In fact, there is a growing body of evidence that indicates that kappa-opioid agonists are actually “aversive”—the opposite of addictive. This is an important advantage over most powerful analgesics currently prescribed. The effectiveness of salvinorin A as an analgesic has been repeatedly demonstrated in animal studies. In my book I include many case reports in which people testify to the effectiveness of this herb for managing pain. The traditional Mazatec use of *Salvia divinorum* to treat headaches and arthritis also attests to its effectiveness as an analgesic.

The ability of salvinorin A to block perception of pain also suggests that it may prove useful as a short-acting general anesthetic. The fact that it does not depress respiration is particularly interesting because it indicates that salvinorin A could be much safer than most general anesthetics currently in use.

Several years ago Dr. Karl Hanes published a case report in the *Journal of Clinical Psychopharmacology*, in which he described a patient that obtained relief from chronic depression by using *Salvia divinorum*. Subsequently he published a paper in the journal *MAPS*, reporting that he obtained similarly positive results when he prescribed the herb to other patients who suffered from clinical depression. In my book I describe dozens of additional accounts of people who have recovered from serious depression with the help of this herb. It is especially interesting that these people were able to obtain persistent relief from their depression after only a few treatments. Quite unlike the continuous medication regime required with conventional antidepressants such as Prozac, which in most cases only offer symptomatic relief from depression, *Salvia divinorum* often produces long-lasting clinical improvement.

Because salvinorin A alters various perceptual modalities by acting on kappa-opioid receptors, it is clear that these receptors play a prominent role in the modulation of human perception. This suggests the possibility that novel psychotherapeutic compounds derived from salvinorin A could be useful for treating diseases manifested by perceptual distortions (e.g., schizophrenia, dementia, and bipolar disorder). This is a promising area of research that is important to pursue further.

Salvia divinorum has several properties that make it useful in psychotherapy: It produces a state of profound self-reflection, it improves one's ability to retrieve childhood memories, and it provides access to areas of the psyche that are ordinarily difficult to reach. I have spoken with several psychotherapists who have used this herb in their practice. They are impressed with its effectiveness as a psychotherapeutic tool. This type of application is not new—the Mazatecs have long used *Salvia divinorum* to treat psychological complaints.

Salvinorin A is also an important neurochemical probe for studying the dynorphin/kappa-opioid-receptor system. As such, it is useful for research into the neurological mechanisms of perception and awareness. Salvinorin A is remarkable in that it belongs to an entirely different chemical class than any previously identified opioid receptor ligand (it is a diterpenoid). This fact is of great interest to pharmacologists because it opens up a vast new area for future drug development.

No potential for long-term abuse

There are many popular misconceptions about *Salvia divinorum*. Presumably, Assembly Bill 259 is based on some of these. Many of these misconceptions have their origin in sensationalistic stories presented by misinformed journalists, and others derive from the absurd advertising claims of unethical herb vendors who market this herb as a “legal high” and deliberately exaggerate its effects to increase sales.

The fact is that the effects of *Salvia divinorum* are not appealing to recreational drug users. The majority of people who try it find that they do not enjoy its effects and do not continue using it. It does produce an altered state of awareness, but does not produce a “high” (i.e., it is not euphoric or stimulating). *Salvia divinorum* produces a state of increased self-awareness. For this reason, some people use it as an aid to meditation, contemplation, and spiritual reflection. There are people who are intrigued by salvia's effects, but even these people use it infrequently. Because it increases self-awareness, it is useless as an escapist drug. When used in a careless manner, it tends to produce unpleasant experiences, and that of course discourages further use (i.e., abuse is self-limiting).

Salvia divinorum is not addictive or habit forming. This has been demonstrated in several animal studies. Its mechanism of action indicates that it may actually be anti-addictive. Many people have reported that *Salvia divinorum* actually helped them to overcome previous substance abuse problems. With funding from the National Institute on Drug Abuse (NIDA), researchers at the University of Iowa are now studying salvinorin A and attempting to develop derivatives that could be useful for treating methamphetamine and cocaine dependence.

Safety

Salvia divinorum is non-toxic. Toxicological studies have been performed by Dr. Leander Valdés at the University of Michigan, Jeremy Stewart at the University of Mississippi, Dr. Frank Jaksch of Chromadex Inc., and Dr. Wayne Briner at the University of Nebraska. Neither *Salvia divinorum* nor salvinorin A showed toxicity in any of these studies. There is a vast body of empirical evidence that indicates *Salvia divinorum* is a remarkably safe herb. Indeed, the Mazatecs, who have probably used *S. divinorum* for hundreds of years, do not attribute any toxic properties to this plant.

Conclusions

Salvia divinorum is an important medicinal herb that has no potential for long-term abuse. It does not present a significant risk to public health or safety. Obviously, there is a problem with young people using this herb (especially when they use it carelessly). There is a sensible way to deal with that problem: regulation that prohibits sale or delivery to minors. This is a useful medicinal herb that enriches the lives of many responsible adults. Since it is by all accounts a remarkably safe herb (when used responsibly), it would be overly restrictive to make it illegal for all citizens. Placing it in Schedule I would deprive people of a safe and useful medicinal herb, and it would seriously hamper promising medical research. Because of its complex stereochemistry, salvinorin A is virtually impossible to produce synthetically. It is important that its source plant, *Salvia divinorum*, remain available so that researchers can continue to study this important compound.

Evidently, this bill is based on inaccurate information about *Salvia divinorum*. Schedule I is intended for substances that have a high potential for abuse, a lack of accepted safety, and no currently accepted medical use. *Salvia divinorum* does not meet any of these criteria.

I appreciate your taking the time to read this letter and acquaint yourself with the facts about *Salvia divinorum*. Please feel free to contact me if I can provide you with any additional information.

Sincerely,

A handwritten signature in black ink, appearing to read "Daniel J. Siebert". The signature is fluid and cursive, with a large initial "D" and "S".

Daniel J. Siebert