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**UNITED STATES DISTRICT COURT
DISTRICT OF OREGON**

THE CHURCH OF THE HOLY LIGHT)
OF THE QUEEN, a/k/a The Santo Daime)
Church, *et al.*,)
Plaintiffs,)
)
v.)
MICHAEL B. MUKASEY, *et al.*,)
Defendants.)
_____)

CIV. NO. 08-3095-PA

**WITNESS STATEMENT OF
THOMAS R. KOSTEN, M.D.**

REPORT OF THOMAS R. KOSTEN, M.D.

I. Introduction

1. My name is Thomas R. Kosten. I am a physician-scientist and clinical psychiatrist. I currently hold the J.H. Waggoner Chair and Professorship of Psychiatry and Neuroscience at Baylor College of Medicine. I am also currently the Mental Health Care Line Executive for the Veterans Administration (VA) in Houston, Texas. I have been hired by the United States Department of Justice at the rate of \$350 per hour of my time to offer my opinion on the practices of the plaintiffs in the case *Church of the Holy Light of the Queen, et al., v. Mukasey*.

2. From 1995 to 2006, I held the position of Professor of Psychiatry and Medicine at Yale University School of Medicine. From 2000 to 2006, I served as Chief of Psychiatry for the VA Connecticut Healthcare System.

3. I am the Research Director of the VA National Substance Use Disorders Quality Enhancement Research Initiative (QUERI) based at the VA in Houston, Texas. I founded the Divisions of Substance Abuse at Baylor and Yale. I direct the NIH Medications Development Centers for substance abuse at Baylor. I have been supported by a Research Scientist Award from the National Institutes of Health since 1987. I have served on national and international review groups for medications development in substance abuse. I have been a Congressional Fellow in the House of Representatives and a visiting Professor in Russia, Germany, Spain, Greece, China, and Canada. I have earned several major awards for clinical research.

4. I am the founding Vice Chair for Added Qualifications in Addiction Psychiatry of the American Board of Psychiatry and Neurology. I am a Distinguished Fellow in the American Psychiatric Association and Fellow of the American College of Neuropsychopharmacology, Past President of the American Academy of Addiction Psychiatry, and Past President of the College on

Problems of Drug Dependence. My recent work includes serving in 2002 and 2003 on the Committee for substance abuse treatments of the National Academy of Sciences, Institute of Medicine, and since 2007 on the FDA Drug Safety and Risk Management Advisory Committee.

5. I am editor of two major journals in substance abuse, and have been on the editorial board of the *American Journal of Psychiatry* and many other major national and international journals in psychiatry, pharmacology and addictions. From my studies in substance dependence including nicotine, post-traumatic stress disorder, and neuroimaging, I have published over 500 papers, books, and reviews. My neuroimaging research includes detecting and treating cocaine-induced cerebral perfusion defects, and using functional MRI to predict pharmacotherapy outcome. My medication contributions include vaccines for cocaine, opiates and methamphetamine, buprenorphine for opioid dependence, disulfiram for cocaine dependence, medications for cocaine-induced cognitive impairment, and combining medications with behavioral treatments such as contingency management for opioid and cocaine dependence.

6. In my 30 years of clinical experience treating substance dependent patients, I have interviewed and treated hundreds of patients with hallucinogen induced psychiatric complications including panic, suicidal behavior, severe depression, sustained visual, auditory and other hallucinations, delusions, depersonalization, cognitive impairment and other less common forms of pathology such as catalepsy. While some of these patients have had symptom resolution within hours or days of hospital care, other patients have had severe and persistent mental illness that is often minimally responsive to the standard anti-psychotic medications used to treat schizophrenia and related psychoses.

7. The history of N,N-Dimethyltryptamine (DMT) research has been relatively long and shown that the range of 4-30 mg given intravenously and 60-100 mg when smoked is

hallucinogenic in humans. Oral ingestion has not been studied, because it would require concurrently using a second drug (a monoamine oxidase inhibitor – MAOI) in order to allow the DMT to be absorbed without being inactivated in the gut. Thus, the formulation of DMT for oral ingestion has not had any human laboratory investigation for medical safety, potential toxicity or enhanced toxicity from combinations of the DMT with an MAOI. It is critical to avoid toxicity from this drug combination, since both agents increase blood pressure and have other cardiovascular effects that can produce hypertensive blood pressure crises from eating various foods and wines when taking an MAOI.

(a) Various hallucinogenic tryptamines and “cyclic tryptamines” or beta-carbolines including ayahuasca were isolated from Central and South American plant sources during the late 1950s and into the 1960s, and animal and human studies were conducted with these agents, particularly DMT. The Controlled Substances Act (1970) placed restrictions and prohibitions on human investigations with such substances, and few studies were done until about 1996 when newer studies of DMT confirmed both its hallucinogenic and cardiovascular effects. Most investigators such as me have not seen the ethical justification for further human laboratory investigations, since these new studies did not suggest any new dose related effects or novel mechanisms of action beyond the already elucidated mechanisms through serotonergic type 2A (5-HT_{2A}) receptors.

(b) Other components of the ayahuasca mixture are beta-carbolines, which possess activity as monoamine oxidase (MAO) inhibitors. The MAO inhibitory effect of the beta-carbolines may simply potentiate the effect of any indolealkylamine hallucinogen present in the ayahuasca admixture by interfering with its metabolism. Studies with individual beta-carbolines, especially under carefully controlled clinical settings, have been very few. The most commonly

occurring beta-carbolines are harmine, harmaline, and tetrahydroharmine. Evidence suggests that harmine and harmaline are hallucinogenic in humans. Like other classical hallucinogens, these beta-carbolines bind at 5-HT_{2A} receptors and, in animal studies, show DMT-like effects. Thus, the ayahuasca admixtures used by the Church will likely have complex and highly variable individual pharmacological effects across different people, which would be extremely difficult to study with appropriate scientific controls, particularly after oral administration, and scientists are not likely to undertake them.

8. While I have not specifically administered DMT to research subjects or patients, I have treated patients whom I suspect had taken DMT or related hallucinogenic alkaloids in this family of drugs. I cannot confirm whether they were under the influence of DMT, because this family of alkaloids are not routinely screened or detected in urine or blood samples that are obtained in the emergency department, where these impaired patients are admitted and their biological samples tested.

9. My detailed curriculum vitae, including all of my publications as well as a listing of all my forensic experience, are attached hereto at Appendix A.

II. Scope of Report

10. I was asked to apply my clinical practice and research expertise in addiction psychiatry to review and evaluate Plaintiffs' ayahuasca consumption. In this report I offer opinions which fall into three primary categories:

- (a) I identify vulnerable populations at high risk for adverse events from ayahuasca consumption.
- (b) I identify behavior posing known and possible but unknown risks associated with ayahuasca use.

(c) I provide rebuttal testimony to the reports submitted by plaintiffs' experts.

11. In preparing this report, the Department of Justice informed me that the Church holds "works" (gatherings at which ayahuasca is consumed) at least three times per month, each work lasts between 5 and 12 hours, and doses of tea are administered as often as hourly at some works, but nearly always more than once per work. I also reviewed the following documents:

- (a) Excerpts from depositions of Jonathan Goldman, Alexandra Bliss Yeager, John Seligman, Mary Row MD, and Ronald Rosen MD;
- (b) Declaration and article of John Halpern, "Evidence of health and safety in American members of a religion who use a hallucinogenic sacrament,"
- (c) Declaration of Nicholas Cozzi PhD;
- (d) Blank general information, medical history and waiver form;
- (e) Robert Gable article, "Risk assessment of ritual use of oral DMT and harmala alkaloids,"
- (f) Medical screening forms from 11 de-identified individuals, referred to as exhibits 1 through 11, and attached hereto as Appendix B.

12. Beyond these exhibits I have relied on the education and training that have, over more than three decades, informed my clinical experience and judgment. Additionally, I have referenced the Pharmacology section of the new, in press edition of the American Society of Addiction Medicine's "Textbook of Addiction Medicine" published by Lippincott Williams & Wilkins. I am the editor for the Pharmacology section of this definitive textbook and, in this report, specifically relied upon the chapter by Richard A. Glennon Ph.D. entitled: The Pharmacology of Classical Hallucinogens and "Designer Drugs."

III. Summary of Conclusions

13. Vulnerable populations at high risk for adverse events from ayahuasca consumption include anyone who has a severe mental illness or is medically unstable. Ayahuasca can produce a serotonin syndrome in subjects who are also taking a wide range of medications, herbal remedies and other substances. These medications are frequently prescribed by family physicians for depression, anxiety, migraine headaches, nausea and pain. Over-the-counter medications and herbal dietary supplements such as St. John's Wort can also be quite toxic in combination with ayahuasca. Comprehensive screening to prevent these individuals from participating in ayahuasca use would require substantially more professionally trained personnel than are evident from Plaintiffs' own testimony as to their screening policy and practices. The neurochemical actions and behaviors associated with ayahuasca use are also problematic, because they reverse the effects of medications used to treat major psychiatric disorders such as schizophrenia and psychotic depressions. The ayahuasca itself is also unsafe because the process to produce it lacks standardization in the dose it produces, and the quality control procedure uses an actively intoxicated "brewmaster" to judge the amount to give to naïve users. Furthermore, multiple doses are given (stacking) at one occasion (works) without any recognition of the differences between individuals in duration of drug actions and both pharmacological tolerance and sensitization. This ignorance can produce substantial toxicity due to overdosing naïve users not only through individual doses being too high, but also through too frequent dosing during a work or over weeks and months of repeated works.

IV. Analysis

A. Vulnerable populations at high risk for adverse events from ayahuasca consumption

14. Vulnerable populations at high risk for adverse events from ayahuasca consumption

include anyone who is medically unstable or has a severe mental illness. Severe mental illnesses include:

- (a) schizophrenia;
- (b) bipolar disorder;
- (c) depression;
- (d) Post traumatic stress disorder (PTSD);
- (e) substance dependence; and
- (f) dementia or delirium.

Several examples of individuals from vulnerable populations were included in the screening forms. The individual in exhibit 3 reported hospitalization for depression. The person in exhibit 11 reported depression and psychiatric treatment. The person in exhibit 1 reported substance abuse and psychiatric treatment, and those in exhibits 2 and 4 also reported substance abuse with few other details. These persons would need follow-up of these reports that should include contact with their providers and obtaining medical records for review before considering giving them ayahuasca to ingest. People with these disorders are stabilized and their symptoms reduced by using medications that competitively block the same brain receptors that ayahuasca stimulates. Because this blockade is competitive, it can be overcome by giving agents such as ayahuasca that act at these same brain receptors (serotonin type 2a). When ayahuasca overcomes this blockade, then the symptoms of these disorders such as schizophrenia, PTSD or bipolar psychosis will become manifest. These symptoms are neither socially adaptive nor pleasant for these patients. Thus, ayahuasca will cause these patients to become psychiatrically unstable and symptomatic and can lead to their psychiatric hospitalization if the person becomes suicidal, homicidal or gravely disabled and unable to care for himself. More tragically, the patient can

become suicidal or homicidal and complete these acts as their medication effects are reversed due to ayahuasca use.

15. Medically unstable conditions are too common to provide a comprehensive listing, but conditions can include:

- (g) significant hypertension (high blood pressure);
- (h) liver dysfunction such as cirrhosis;
- (i) brain infections such as AIDS;
- (j) gastrointestinal disorders such as weakened muscles or varicose veins in the esophagus leading to bleeding induced by the vomiting;
- (k) endocrinopathies such as adrenal tumors or thyroid dysfunction; and
- (l) a variety of orthopedic abnormalities and chronic pain conditions that are associated with use of prescription opiates.

Several examples of persons with these types of disorders were described in the medical screening forms presented to me. The person in exhibit 8 was taking Benicar for hypertension. The person in exhibit 1 was taking hydrocodone (Norco) for back pain. Opiates can have significant interactions with MAO inhibitors in producing seizures and other toxicity.

16. As elaborated in the next section, ayahuasca has a high potential for producing a serotonin syndrome either on its own or in combination with a wide range of medications, herbal supplements and other substances. This serotonin syndrome increases blood pressure and for a patient with already elevated blood pressure the further increase raises the potential for stroke and myocardial infarction (heart attack). Cirrhosis and other liver dysfunction will impair the ability of the patient to de-toxify the active drugs in ayahuasca and enhance its toxicity. Brain infections such as AIDS can have similar complications to those indicated above for the

psychiatric disorders. Endocrinopathies of the adrenal and thyroid (hyper-thyroid) can produce significant cardiovascular toxicity that will be potentiated by the MAO inhibitor and the DMT in ayahuasca. The person in Exhibit 3 indicated a thyroid condition that would need follow-up before ingesting ayahuasca. Finally, any pain condition where opiates are prescribed, as indicated for the person in Exhibit 8, has the potential for severe drug interactions with ayahuasca, due to the serotonin syndrome as detailed below.

17. The serotonergic actions of ayahuasca are substantial and can produce a serotonin syndrome in Church participants (Boyer 2005). A serotonin syndrome is particularly likely in those who are taking a wide range of medications and other substances that are not typically considered medications such as over the counter remedies, herbal supplements and illicit drugs. The person in exhibit 7 indicated use of herbs and marijuana. It is important to note that several of the Church participants had significant histories of substance dependence (see exhibits 1, 2, and 4). A serotonin syndrome involves symptoms ranging from restlessness and rapid heartbeat to muscle rigidity, seizures and severe blood pressure changes that can result in stroke or myocardial infarctions (heart attacks) and rapid death, if untreated. The potentially interacting medications importantly include standard serotonin reuptake inhibitors (SSRI) such as fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil) and several other related medications for treatment of depression, anxiety, post traumatic stress disorder (PTSD) or substance dependence. Overall, many individuals are prescribed these SSRI medications by their family physicians and do not consider these medications as treatments for psychiatric conditions and would not mention them in the screening forms that are used by the Church.

18. Furthermore, the vulnerable population is even much larger among individuals who would consider themselves relatively healthy adults without psychiatric disorders. For example,

many other medications have substantial risks of precipitating serotonin syndromes. The psychiatric medications include trazodone (Desyrel), venlafaxine (Effexor) (person in exhibit 9 was taking Effexor), bupropion (Wellbutrin, Zyban) (person in exhibit 8 had recently stopped Wellbutrin), isocarboxazid (Marplan), phenelzine (Nardil). Pain medications include fentanyl (Sublimaze), meperidine (Demerol), pentazocine (Talwin) and tramadol (Ultram). Anti-nausea medications include granisetron (Kytril), metoclopramide (Reglan) and ondansetron (Zofran), and anti-migraine medications include almotriptan (Axert), naratriptan (Amerge), sumatriptan (Imitrex) and zolmitriptan (Zomig). Over-the-counter cough and cold medications containing dextromethorphan (Robitussin DM, Sudal DM) have high risks of producing a serotonin syndrome in combination with ayahuasca. Illegal drugs such as Ecstasy, LSD and Syrian rue and herbal dietary supplements such as St. John's Wort and ginseng also can precipitate serotonin syndromes. At least one person (in exhibit 7) indicated use of unidentified herbs that would need follow-up and precise identification before considering ingesting ayahuasca. While this is not an exhaustive listing of potentially interacting medications and herbal supplements, this listing well illustrates what a wide range of hundreds of substances and common conditions such as migraine headache, back pain, and the common cold could lead to toxic and potentially fatal complications.

19. A comprehensive screening for these vulnerable populations would need to be extensive and include hundreds of substances in order to cover all the medical conditions, medications and other commonly used substances listed above. This screening would include psychiatric evaluation, consultation with any treating physicians and obtaining relevant medical records including hospitalizations. Furthermore, this screening would need to be conducted by a highly qualified health care provider who had simultaneous access to a powerful computerized database

of interactions between ayahuasca and all these medical conditions and medications and other substances. Some of these potential drug and medication interactions are detailed further in the Robert Gable article, "Risk assessment of ritual use of oral DMT and harmala alkaloids." In the absence of such a comprehensive screening, the risk from using ayahuasca is significant for a serotonin syndrome with the potential for a fatal outcome.

B. Behavior posing risks associated with ayahuasca use

20. The behavioral effects associated with ayahuasca use include a wide range of hallucinogen induced abnormalities in sensations and perceptions. The behaviors include panic, severe depression, sustained visual, auditory and other hallucinations, delusions, depersonalization, cognitive impairment and other less common forms of pathology such as catalepsy. These behavioral abnormalities can be quite severe and debilitating and lead to psychiatric emergencies such as suicidal or homicidal behaviors, and grave disability to care for oneself including eating, dressing, washing or communicating with others for the necessities of shelter and avoidance of harm.

21. While subjects can have symptom resolution within hours or days, other subjects will develop severe and persistent mental illnesses that are often minimally responsive to standard anti-psychotic medications used to treat schizophrenia and related psychoses. Even the medical profession has had difficulty in identifying specific individuals who will develop these severe and persistent abnormalities after hallucinogen exposure. Therefore, a person with little or no medical training will not be able to screen for the individuals at high risk for these severe and persistent behavioral abnormalities. The statements on page 12 of the Seligman deposition and on page 25 of the Rosen deposition indicate that the screening procedures and personnel are not adequate to identify individuals at high risk for adverse behavioral outcomes from ayahuasca use.

22. The medical profession has difficulty in identifying every individual who will develop these severe and persistent abnormalities after hallucinogen exposure. Thus, if the prospective user belongs to any of the vulnerable groups described above, the advice to them has been to avoid using these drugs. If these drugs are used at all, then the dosage and frequency of usage should be minimal and regular usage minimized.

23. A particular problem with using ayahuasca in the manner described for this organization is that the dosage could be highly variable, since there is neither control over the extraction process nor scientific monitoring of the concentration of the drug that might be in any particular preparation. The suggested "quality control" of the drug product using an experienced user to test the strength of the brew produced at a "works" is extremely unreliable. Furthermore, no standards insure minimal safety for other individuals who will be then taking the same brew, particularly individuals who have never taken ayahuasca or whatever active agents the brew might contain on that particular occasion. Thus, medical safety is compromised and potentially non-existent due to this great variability in doses and unreliability of the subjective quality control that relies on intoxicated active users to judge the quality, toxicity and safety of that day's brew for naïve or even experienced users.

24. The variability is not only a problem for an individual's initial exposure to these drugs, but also for the repeated exposure to these drugs, since a dose of the drug could be substantially greater at later exposures and have many more adverse effects than a previous dose.

(a) During a particular work the practice of stacking doses over time will lead to a substantial enhancement of effects depending on the half-life of the brew in that particular individual. The half-life is how long it takes for the blood and brain levels of the DMT and harmaline to drop to half of their peak levels after ingestion. This half-life will not be the same for every individual. If the half life of ayahuasca for the "taster" or brew-master for that day is

substantially shorter than for the other participants, particularly for a new participant, then the new participant will accumulate much higher blood and brain levels of the drugs than will the "taster" or brew-master for that day. Since the brewmaster decides the time intervals between additional doses or stacking of the drugs, the new participant may become significantly more intoxicated and ill than the brewmaster.

(b) This variability will occur not only during a particular Church "work," but across time at different "works." Thus, with weekly drug exposures two very different pharmacological effects can occur – tolerance and sensitization. Some individuals will become tolerant and get less effects and shorter duration of effects over weeks of use when using the same dose of drug. Tolerance can be a particular problem because the reinforcing effects of drugs tend to tolerance and lessening over time. Thus, the experienced brewmasters are likely to have substantially more tolerance to the sought after effects of DMT and thereby recommend greater doses than naïve users would otherwise need or use to attain that same reinforced or desired state on their own.

(c) Other individuals develop predominant sensitization to the drugs where their response to the drugs increases as they use it repeatedly over weeks or months. For these individuals the repeated weekly use over months will increase their potential for adverse effects either during intoxication or after discontinuation. Sensitization is frequently evident with serotonergic hallucinogens such as ecstasy (MDMA), as well as amphetamine, cocaine and alcohol. Seizures, panic attacks, paranoia and other adverse effects of drugs typically follow a pattern of sensitization over weeks and months of use.

C. Rebuttal of plaintiffs' expert reports

24. Many of the effects of these drugs are subjective and require very well trained observation, which is not evident in these expert reports. While one of the experts has clinical

credentials and has been trained to detect and diagnose psychiatric pathology, another expert is a pharmacologist who works only with animals and chemicals and has no clinical experience to describe or assess the effects of these drugs. Furthermore, the credentials for the plaintiff's clinical expert in this area of addictions treatment and psychopharmacological research are not well established within the scientific community.

(a) Dr. Halpern's statement and CV indicate no experience treating patients with substance dependence or use of these hallucinogenic drugs after his residency. He specifically offers no basis in clinical experience for his opinions of safety with ayahuasca use in humans. The only observation of ayahuasca use in humans that he cites is his retrospective interviews of Church members' uses. He cites being a research assistant for data collected as part of a study conducted by Strassman as evidence of his experience with this field. This experience appears to have occurred during his residency in medicine and that supervised employment experience is quite different from primary responsibility for designing, conducting, analyzing and reporting a complex clinical study. His role at that time in collecting data under supervision might have been influenced by many factors, but was not informed by the clinical training needed for the subtle observations and clinical insights that are essential for detecting and appropriately diagnosing disorders induced by hallucinogens. This experience of Halpern also was not informed by following these persons through real life rather than through their own self-reports of acute experiences or their personal assessments of their life accomplishments related to using these hallucinogens.

(b) In contrast, my day-to-day professional medical experience in clinical settings with substance abusers for over 30 years gives me knowledge of consequences that Halpern, and of course Cozzi who has no clinical experience, fail to consider. A few examples of my clinical

experience observing adverse effects of DMT-like hallucinogens include several young men and women who used these drugs as infrequently as 10 times or as often as 400 times. I first met these patients in the emergency department after they had a "bad trip," as it was called. Some were very agitated and terrified, while others were mute and apparently unseeing and completely drawn within themselves. More importantly these young persons did not recover back to normal after a day or two. They were all hospitalized for weeks and treated with antipsychotic agents in attempts to get their behavior and ability to concentrate normalized and for many to help them recover from suicidal plans as their concentration and insight improved. These young people felt that their lives were ruined and not worth living. Many described their lives as filled with flashbacks of their bad trip when using the hallucinogen. I followed several of these very sad persons for many years in New Haven. Their lives were extremely constricted with very limited social activity and days filled with smoking cigarettes and watching television or just sitting outside staring off into empty space. When I spoke to these now chronic psychiatric patients over their years of treatment and attempts at rehabilitation, they often had rather glowing memories of their hallucinogen experiences as the best time in their lives and as a time when they had excitement and stimulation that was now lost. When they occasionally attempted to recapture that exciting time by using these drugs again, the results were disastrous and resulted in re-hospitalization for re-stabilization of their psychosis. Overall, chronic hallucinogen users have shown little ability to recall the terrible aspects of their illness, but selectively remember only some broadly exciting aspect of the drug use. This aspect of selective positive memories in hallucinogen users is commonly found in clinical situations, and is not being considered by these experts in their somewhat naïve recording and interpretation of the data that they present.

(c) In summary, the Plaintiffs' health experts have not sufficiently examined the issues involved in ayahuasca use to fully understand the range of possible health consequences from ayahuasca use. In particular, they have not interviewed or had experience with the human causalities resulting from hallucinogen use and not followed these patients over the years necessary to understand how bad the outcomes can become with the development of chronic psychoses. The evidence in Halpern's study that many Church members met lifetime criteria for psychiatric disorders makes these relatively positive self-reports about the personal benefits of hallucinogen use with ayahuasca particularly suspect and raises significant risks for participants in this Church based on the poorly developed screening procedures of this Church.

25. Other well established experts in this field have observations that do not agree with the conclusions of the Plaintiffs' expert reports.

(a) Several of the relevant experts including Brimblecombe & Pinder or Hollister, who are cited in the Chapter from the ASAM book that I edit do not concur with the clinical judgments of Dr. Halpern. Those authors who do concur with Dr Halpern's clinical judgments – for example, Shulgin – are not clinically trained and their rather positive descriptions of the effects of these drugs on themselves and their co-users are considered non-objective and scientifically suspect in the larger scientific and addiction treatment community.

(b) Furthermore, the MAOI agent required for oral use of ayahuasca has the potential for harmful effects, which these expert reports have not considered. The combination of MAOIs with a variety of foods including cheeses and wines can produce severe hypertensive crises, where blood pressure rises to sufficient levels to produce strokes and myocardial infarctions. The ayahuasca-induced blockade of MAO allows a larger quantity of serotonin to accumulate in nerve terminals. Excessive accumulation can produce a range of adverse physiological

symptoms, a "serotonin syndrome" that includes tremor, diarrhea, autonomic instability, hyperthermia, sweating, muscle spasms and possible death (Boyer 2005). These cardiovascular effects will be amplified by the 30% increase in heart rate and 35 mmHg increase in systolic and 30 mmHg increase in diastolic blood pressure induced through the DMT in ayahuasca (Strassman 1994). The potential for lethal toxicity is illustrated by a 25-year-old man who died from ingesting ayahuasca (Sklerov 2005). Thus, these two agents have a combined cardiovascular toxicity that is not addressed in the assessments of these expert reports.

26. The report from Halpern includes a variety of inaccuracies and misstatements as well as simple lack of logic.

(a) The statement on Page 5, last paragraph is inaccurate: "there is virtually no possibility of a human being consuming a sufficient quantity of the Daimé to cause any immediate toxic or lethal effect." Similar to my critique for Cozzi below, Halpern appears to assume that vomiting would terminate the use of ayahuasca. However, many abused drugs can produce nausea and vomiting such as opiates, which typically induce vomiting among many naïve users and abusers. Nevertheless, these opiate users will ingest sufficient amounts of opiates to produce respiratory arrest and other severe toxicities. As the reports from these Church members indicate, these Church participants do not terminate their use of the tea after an episode of vomiting, but continue to use it after their vomiting subsides. The repeated use after vomiting also is supported and encouraged by the brewmaster at the Church works. Since the vomiting subsides after a relatively brief period of time compared to the duration of action for oral DMT, significant DMT and MAOI toxicity is possible from the accumulating dose of these two drugs from repeatedly drinking the tea. The vomiting would not lead to "virtually no possibility" to consume enough of this tea to experience toxicity.

(b) An example of illogic occurs on Page 6, second to last paragraph: "the consumption of Daime as a sacrament is literally then the non-drug use of DMT." This statement is simply meaningless. Nothing in the word sacrament literally translates into "non-drug use of DMT."

(c) Another example of illogic with no support in the typical use of science or the scientific methods occurs on Page 6, last paragraph: "It is scientifically inappropriate to refer to Daime as a hallucinogenic drug as compared to synthetic DMT." Daime is DMT, and DMT is a hallucinogenic drug. Thus, Daime is a hallucinogen drug. That is simple pharmacology and the most simple of logic.

(d) The following statement on Page 7, first paragraph has nothing to do with science and seems to just be an opinion with no substantiation: "Ingestion of Daime to 'get high' is anathema to members and especially the leadership of Santo Daime, who consider the protection of Daime for only proper sacramental purposes as one of their highest responsibilities."

(e) As I had indicated above, the statement on Page 7, last paragraph has no basis in scientific facts or interpretations: "Indeed, the use of the term 'hallucinogen' is both misleading and inaccurate when describing sacramental peyote use as well as sacramental Daime use." Daime is a hallucinogen and calling it sacramental does not change that pharmacological quality of this chemical entity.

(f) The following statements on Page 9, second paragraph about medical consequences of hallucinogen use are simply wrong and seem to reflect lack of clinical experience: "Serious medical consequences from ingestion are the rare exceptions with all hallucinogens and physical trauma is typically secondary to activities performed while under the influence of the drug. Moreover, when a cardiovascular or other serious medical condition arises

post hallucinogen ingestion, emergency medical teams generally correctly presume that the individual has taken a compound adulterated with a dangerous non-hallucinogenic substance.” In particular, DMT and the associated MAOI in this drug combination have substantial and well documented cardiovascular effects that are detrimental to a wide range of vulnerable humans and are potentially fatal in those taking medications for medical conditions that I have outlined previously in this report. The medical conditions and medications are not adequately screened out through the procedures detailed in any of the reports or exhibits that I examined.

(g) The statement on Page 9, last paragraph specifically addressed physical dependence as if it were the only part of dependence and his statement ignores the psychological aspects of dependence; this statement is simply not true for a wide range of psychoactive drugs: “The psychoactive substances such as Daimonite and peyote are not known to induce physical dependence. Tolerance is quite rapid, precluding a theoretical scenario in which daily ingestion (which is not a feature of either religion) might lead to physiological dependence.” Psychological aspects of dependence including craving, inability to stop use in spite of harmful consequences in health, social activities or psychological symptoms are all part of the DSM-IV criteria for dependence and abuse. Physical symptoms of withdrawal are not required, but tolerance, which does occur to these drugs as is indicated by Halpern in this statement, is a part of the diagnostic criteria for dependence.

(h) The following statement on Page 9, last paragraph emphasizes the point of why there is such a great risk with this drug combination, because there are no directions on how these drugs might be used safely: “There are, of course, risks associated with the ingestion of virtually every chemical substance, including those available over the counter, particularly when they are not utilized according to directions.” Thus, the risks are essentially unknown for using

these drugs in the way that this Church exposes people. However, the potential risks are substantial based on solid clinical experience and experimental pharmacological data in humans.

(i) The statement on Page 10, first paragraph indicates that Halpern has a very inadequate understanding of what needs to be done for appropriate screening of risk in medical practice and that he does not know the details of what is actually being done by these Church leaders: “the Santo Daime Church has developed a form entitled ‘Confidential Medical Record’ that it proposes to use prior to permitting any participation in Church activities where the Daime might be consumed. These forms are structured to carefully screen for a variety of medical and psychiatric conditions that can then be reviewed by a physician should there be any questions about risks to physical or mental health. The documents clearly indicate that should there be any question about health, a new physical and access to medical and psychiatric records could be requested by Church officials. For example, the form asks individuals if they have ever taken certain psychotropic medications and whether they ever required a psychiatric hospitalization, and this question does provide an indirect way of inquiring about remote major psychiatric illness and psychotropic medication use.” As I have detailed in other sections of this report, we have more than sufficient evidence that none of these precautions are undertaken by the Church leaders to meet the standards of basic medical and psychiatric safety. Instead, some vulnerable persons appear to have been deliberately exposed to a potentially toxic drug combination.

(j) The statement on Page 11, first full paragraph has no basis in scientific facts or in any data collected in a scientifically credible manner: “The empirical evidence to date fails to establish any threat to individual or long-term health issues but does point to relative safety and possible additional physical and mental health benefits.” Scientific data are collected based on a hypothesis; the data collected must constitute a sample size adequate to prove or disprove that

hypothesis. None of those procedures were followed for the empirical evidence that appears to be cited in this statement.

(k) The conclusion on Page 11, first full paragraph is simply in error and ignores the available clinical and pharmacological data that do provide some direct and scientifically credible evidence to the contrary of this statement: "Absent direct evidence that the Daime is a serious health risk, and such evidence does not currently exist, there appears to be no scientific or medically valid reason to prohibit its ingestion as a bona fide religious sacrament."

(l) Finally, the conclusion on Page 11, first full paragraph has no basis in scientific fact and appears to be contradicted by those limited data that are scientifically and clinically sound: "In this regard then, there are no public health concerns that would justify criminalizing the Santo Daime's use of their ayahuasca sacrament, Daime."

(m) In summary, the statements made in this report by Halpern have many inaccuracies and points of illogic. His conclusions based on these inaccuracies and illogical inferences are both incorrect and dangerous to the health of many vulnerable people.

27. The report from Cozzi includes several assumptions about human behavior and effects of hallucinogens that indicate his lack of clinical experience with these individuals or these drugs.

(a) For example on Page 4, first paragraph he states, "The potential to consume a toxic amount of Daime tea is, however, practically nonexistent for the following reason: Daime typically produces nausea and vomiting in the amounts consumed for religious purposes. This naturally limits the amount of Daime that can be ingested; the purging effect makes it virtually impossible for a human being to consume enough Daime tea to experience toxicity. This is in contrast to most other substances taken by mouth, including over-the-counter and prescription drugs, where such a fail-safe mechanism does not exist." Many abused drugs can produce

nausea and vomiting, such as opiates, which typically induce vomiting among many naïve users and abusers. Nevertheless, despite experiencing nausea and vomiting, these opiate users will ingest sufficient amounts of opiates to produce respiratory arrest and other severe toxicities. As the reports from these Church members indicate, these Church participants do not terminate their use of the tea after an episode of vomiting, but continue to use it after their vomiting subsides. The repeated use after vomiting also is supported and encouraged by the brewmaster at the Church works. Since the vomiting subsides after a relatively brief period of time compared to the duration of action for oral DMT, significant DMT and MAOI toxicity is possible and would not be making it “virtually impossible” to consume enough of this tea to experience toxicity.

(b) A further example of a misstatement occurs on Page 4, second paragraph: “As it true: for many pharmacologically active substances, there may be interactions between Daime and other medications. . . . I am informed that the Santo Daime Church leaders are carefully trained to obtain information from prospective church members before administering Daime to prevent such drug interactions from occurring.” This information from the Church leaders is grossly misleading or is misinterpreted by Cozzi perhaps due to his lack of clinical experience. As detailed previously in this report, the screening procedures are not conducted by carefully trained leaders of the Church, but are done by persons with no clinical credentials. Furthermore, these evaluations show no evidence of a professional review or consideration of toxic medication interactions with these drugs. Several medications are listed on the screening form exhibits, which could have significant interactions with these drugs; and no indication is given that any actions were taken by the Church leaders to prevent drug interactions from occurring in the persons who completed these forms indicating their use of these medications.

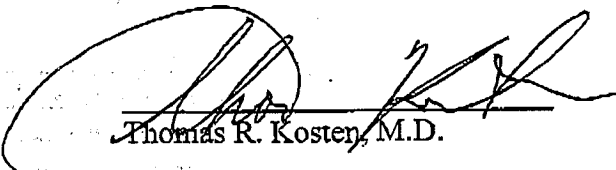
28. As a scientific and medical journal editor for the past 20 years, I can judge that the data presented in the plaintiff's expert reports do not meet minimal standards of scientific objectivity. I would further challenge the ability of other investigators to replicate the observations of Halpern's 2008 study in an unbiased and controlled manner. The required studies of these hallucinogenic compounds are quite difficult to complete in humans, but minimally require control of the dose given and the frequency of dosing, and objective and blinded recording of subjects' responses to a placebo as well as the active drug. Because the responses need to be assessed in a blinded manner with some type of a placebo control, it would be necessary to use an active placebo that would also induce the nausea and vomiting that ayahuasca induces as well as reproducing the foul smell that these teas typically produce. Thus, these anecdotal reports that have been used as data for drawing conclusions about the safety and toxicity of these drugs are seriously lacking in scientific credibility and do not meet the standards for making informed decisions about these drugs and either their short term or long term effects in vulnerable or even normal individuals.

29. The Plaintiffs' experts have limited credibility as sources of scientific information or conclusions. Their statements are not based on clinical observations of hallucinogen and DMT users who have had serious medical or psychiatric complications and instead are based on unverifiable self-reports of individuals who suffer from a condition of inaccurate perceptions and memories that are induced by these drugs. This clinical observation of hallucinogen effects on recall and the related affective content of that recall is well documented in the literature, including in a book about this area by Malcolm Bowers, M.D., a famous psychiatrist, professor and scientist at the Yale University Departments of Psychiatry and Pharmacology, who wrote very cogently and clearly about these chronic effects of hallucinogens in the 1970's. The health

risks are very real and severe. The Plaintiffs' experts appear not to have the clinical experience or knowledge that is relevant to this critical area of human pharmacology. I hope that their misinformation does not force us to relive and relearn a terrible time in U.S. history of hallucinogen drug abuse from nearly 40 years ago.

30. Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

DATED: December 6, 2008



Thomas R. Kosten, M.D.

References

- Boyer E.W., Shannon M. The serotonin syndrome. *N Engl J Med* 2005; **352**: 1112–20.
- Brimblecombe RW & Pinder RM. *Hallucinogenic Agents*. Bristol, England: Wright-Scientifica, 1975.
- Hollister LE. *Chemical Psychoses*. Springfield, IL: Charles C. Thomas, 1968.
- Morris K. Research on psychedelics moves into the mainstream. *Lancet* 2008; 371:1491-1492.
- Shulgin AT & Shulgin A. *Tihkal*. Berkeley, CA: Transform Press, 1997.
- Sklerov J., Levin B., Moore K. A., King T., Fowler F. A fatal intoxication following the ingestion of 5-methoxy-*N,N*-dimethyltryptamine in an ayahuasca preparation. *J Anal Toxicol* 2005; **29**: 838–41.
- Strassman RJ. Human psychopharmacology of *N,N*-dimethyltryptamine. *Behavioral Brain Research* 1996; 73(1-2):121-124.
- Strassman R., Qualls C. R. Dose–response study of *N,N*-Dimethyltryptamine in humans: I. Neuroendocrine, autonomic, and cardiovascular effects. *Arch Gen Psychiatry* 1994; **51**: 85–97.