

STATEMENT OF NICHOLAS V. COZZI, Ph.D.

1. My name is Nicholas Vito Cozzi. I have previously submitted a declaration for the Church of the Holy Light of the Queen (CHLQ) regarding pharmacological and toxicological issues surrounding the sacramental use of the Daime tea. Daime tea is also known as "ayahuasca"; both terms will be used in this document.
2. I have been asked to review and comment on reports made by Drs. Jerry Frankenheim, George Glass, Donald Jasinski, Thomas Kosten, Srihari Tella, and Alexander Walker. Several of these reports suggest that data obtained with LSD can be extrapolated to Daime. Because there is much repetition in the defendants' expert reports, the following discussion will mainly focus Dr. Frankenheim's lengthy declaration.
3. Dr. Frankenheim repeatedly conflates Daime with DMT and DMT with LSD and states that it is "reasonable and necessary" to apply knowledge of LSD to DMT. He states that it is "valid to predict that the consequences of DMT usage are similar to the consequences of use of the better characterized hallucinogens like LSD". Dr. Frankenheim cites a study (Riba et al., 2003) to support his statement that "Subjects given Daime reported the same psychological and somatic effects, qualitatively and quantitatively, as those of LSD". However, the Riba study did not compare Daime with LSD and no reports exist that have specifically compared the effects of Daime with either LSD or DMT. What does the available scientific evidence actually show?
4. The Riba study cited above employs self-reported psychometric scales to evaluate subjective effects to Daime. These scales included the Hallucinogen Rating Scales (HRS, incorporating 6 scales) and the Addiction Research Center Inventory (ARCI, incorporating 5 scales). Neither the HRS nor the ARCI was specifically designed to evaluate Daime. The HRS was designed to assess the subjective effects of intravenous DMT in humans (Strassman et al., 1994) and the ARCI was designed to assess a range of physical and subjective effects of drugs from various pharmacological classes (Haertzen, 1966). When the reliability of the HRS was tested in Daime users, only four of the six HRS scales showed an acceptable level of internal consistency (Riba et al., 2001a). Therefore, it is unlikely that the HRS accurately reflects the subjective effects of Daime to a reasonable degree of certainty. The HRS has not been validated for any other hallucinogens, in particular LSD. It has never been used or validated as a tool to compare the subjective effects of Daime with DMT, DMT with LSD, or Daime with LSD. It is pure speculation that a positive HRS response establishes that Daime is "like" DMT or LSD.
5. The ARCI is a 550 item true/false questionnaire that attempts to assess the acute physical and subjective effects of a wide variety of drugs including alcohol, psychostimulants, opioids, sedatives, and hallucinogens (Haertzen, 1966; Fischman and Mello, 1989). The ARCI is divided into five subscales (A, BG, MBG, LSD, PCAG) designed to respond to certain drug effects. For example, the ARCI-A scale measures subjective feelings of "intellectual efficiency and energy"; increases in the ARCI-A subscale are seen with amphetamine (Adderall®) or methylphenidate (Ritalin®), for instance. The ARCI-MBG scale is a measure of euphoria; increases in this scale are seen with many different prescription and nonprescription drugs such as alcohol, amphetamine (Adderall®), barbiturates, marijuana, and pentazocine (opioid analgesic; Talwin®) (Fischman and Mello, 1989). The ARCI-LSD scale is a measure of dysphoria, fear, somatic complaints, and paranoia (not hallucinogenic effects, as one might infer from its name) (Haertzen, 1966; Haertzen, 1974). Like the ARCI-MBG scale, ARCI-LSD increases are observed both with prescription and nonprescription drugs with many different pharmacological effects including caffeine, dextromethorphan (antitussive; Robitussin Cough Calmers®), diphenhydramine (antihistamine; Benadryl®), scopolamine (anti-

motion sickness; Transderm Scop®), nalorphine (opioid antagonist; Lethidrone®), and pentazocine (opioid analgesic; Talwin®), for example (Fischman and Mello, 1989; Preston and Walsh, 1997).

6. When Daime users were administered the ARCI test, increases in three of the five ARCI subscales, the ARCI-A, the ARCI-LSD, and the ARCI-MBG subscales, were observed (Riba et al., 2001a; Riba et al., 2001b; Riba et al., 2003). Because many different drugs known to have very different psychoactive effects can all produce changes in these three scales (see preceding section), it follows that the subscales cannot establish that Daime is "like" LSD anymore than they can establish that caffeine is "like" LSD or that Benadryl® is "like" LSD. The conclusion is that, at best, the HRS and the ARCI are imprecise measures of human psychoactive drug experience and it is therefore premature and scientifically unsound to infer that the effects of Daime are "like" the effects produced by LSD or DMT using these measures. Dr. Frankenheim's assertions in this regard are not supported by the scientific evidence.
7. Although Daime may mimic *some* of the effects produced by LSD and other hallucinogens, the scientific evidence shows that it may also produce effects that mimic some effects associated with Talwin® or Benadryl®. However, the unique effects produced by Daime are easily distinguished by human beings from the states produced these other substances. As a trivial example, the time course of the Daime effect is perhaps 3-4 hours whereas LSD produces effects lasting 8-10 hours and the effects of DMT are dissipated within about 45 minutes. More to the point, human subjects report that Daime evokes effects that are quantitatively and *qualitatively* different, at least, from DMT. Subjects described the Daime effects as similar to dreaming (Riba et al., 2001b). Effects are reported to be of milder intensity, slower onset, and a longer overall duration than the effects experienced with DMT alone (Grob et al., 1996; Callaway et al., 1999; Riba et al., 2003).
8. Dr. Frankenheim makes numerous references to neurotransmitter receptor binding profiles in attempting to conflate Daime with DMT and LSD. He focuses exclusively on serotonin 5-HT1A and 5-HT2A receptor subtypes, and presents an overly simplistic neuropharmacological model for the psychological effects of LSD and DMT.
9. However, LSD and DMT also act at numerous other receptors, not just the serotonin 5-HT1A and 5-HT2A receptor subtypes. These other receptors include the following: 5-HT1B, 5-HT1D, 5-HT2B, 5-HT2C, 5-HT3, 5-HT6, 5-HT7, alpha adrenergic, beta1 adrenergic, beta2 adrenergic, dopamine D1, D2, D3, D4, D5, and histamine H1. It is known that the complex behavioral effects of LSD and DMT are mediated by these other receptors, in addition to the 5-HT1A and 5-HT2A receptor subtypes. For example, some of the behavioral effects of LSD depend on dopamine D2 receptor activation (Marona-Lewicka et al., 2005). Dr. Frankenheim's explanation of the roles of various neurotransmitter receptors in mediating the psychoactive effects of these compounds is faulty and incomplete.
10. In addition to the above list of receptors, DMT also binds to the serotonin 5-HT1E receptor, the kappa opioid receptor, the dopamine uptake transporter (DAT), and the serotonin uptake transporter (SERT) (Cozzi et al., 2008a; Cozzi et al., 2008b, National Institutes of Mental Health Psychoactive Drug Screening Program; see <http://pdsp.med.unc.edu/>). LSD, on the other hand, is not known to bind to these receptors or transporters. My colleagues and I have recently shown that DMT also binds to the sigma-1 receptor, that it modulates sodium ion fluxes via a sigma-1-regulated sodium channel (hNav1.5), and that at least some of the behavioral effects of DMT in animals are mediated through the sigma-1 receptor (Johannessen et al., 2008). See Appendix 1 for detailed information.
11. In summary, the receptor binding profiles of DMT and LSD are far more complex than described by Dr. Frankenheim; it seems that Dr. Frankenheim is attempting to "square the circle". It is expected

that the receptor binding profile for ayahuasca would be even more complex than the profiles of either DMT or LSD because of the presence of other substances within ayahuasca.

12. Dr. Frankenheim states that it is not possible to establish a "safe" dose of Daime. In fact, centuries of ayahuasca use have empirically established that people can consume Daime in quantities sufficient to produce the desired effects sought by sacramental users and which do not produce overt toxicity. There are neither anecdotal reports nor credible medical or scientific reports that the sacramental use of Daime poses significant health risks.
13. Consumption of Daime commonly produces nausea and vomiting. This is not considered an adverse reaction by Daime users and is instead considered to be beneficial in that it is believed that toxins are being purged from the body. The biological basis for the nausea and vomiting associated with Daime has not been studied, but a partial explanation may be that the substances in Daime active serotonin 5-HT<sub>3</sub> and dopamine D<sub>2</sub> receptors in the chemoreceptor trigger zone and vomiting center in the brainstem (Sleisenger, 1993). It is also possible that gastrointestinal mechanisms may be involved. Vomiting is generally not a medical concern, unless it is prolonged and excessive, which could lead to dehydration and electrolyte depletion. This is easily correctable. Repeated or profuse vomiting could cause erosions or surface tears in the esophagus. Aspiration of gastric contents would not be anticipated to be of concern because the pharyngeal (gag) reflex will prevent this from occurring, and Daime is not known to inhibit this reflex.
14. Dr. Frankenheim suggests that the Judeo-Christian use of wine (containing the drug ethanol) is not pharmacologically active and implies that wine use in this context is therefore not defined as drug use. (Section II. 7.) He may be referring to *Christian* rituals (e.g. Catholic mass) in which a few sips may be consumed. On the other hand, for the Jewish Passover Service *four cups* of wine (enough to be psychoactive in most persons) are intended to be drunk by all participants as instructed in the Passover Haggadah. Regardless, a drug is never defined on the dose consumed in a specific situation; whether or not a substance "is intended to be pharmacologically active" is irrelevant to its identity as a drug.
15. According to the Federal Food, Drug, and Cosmetic Act (SEC. 201. [21 USC 321], "drug" means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C).
16. Thus, because wine used in Judeo-Christian rituals contains the drug ethanol, it too is a drug, regardless of whether a participant in such a ritual intends to become inebriated or in fact becomes inebriated after consuming it.
17. Although wine contains ethanol and is therefore a drug, the use of wine in the context of a religious ceremony is considered sacramental (i.e. "nondrug") use. Typical societal legal proscriptions against alcohol consumption (e.g. by persons under 18 years of age) are suspended because of the religious context of wine consumption. Likewise, while peyote use outside of Native American religious ceremonies is prohibited by law, peyote consumption within these ceremonies ("nondrug" use) is protected by law. This religious use is indeed defined as "nondrug" use in the Code of Federal Regulations (21 CFR 1307.31).

18. Dr. Frankenheim assumes as a "given" that users of Daime seek a "psychosis-like" effect. (Section II. 5.) Dr. Frankenheim repeatedly refers to the psychological states induced by hallucinogens in pejorative language such as "psychotomimetic", "psychosis-like", "mental distortions", etc. These terms all have a negative, pathological flavor and Dr. Frankenheim implies that the state induced by Daime is itself negative or pathological. These statements and similar ones in his declaration belie his understanding of Daime use; in reality, sacramental users of Daime seek spiritual or religious fulfillment, not psychosis.
19. The term "psychotomimetic" was coined in the 1950s when the pharmacological distinctions among psychoactive compounds that disrupted normal, waking consciousness in a variety of ways were not well-understood. The term "psychotomimetic" was indiscriminately applied to various drugs such as LSD, anesthetic agents such as phencyclidine (PCP) and ketamine, and anticholinergic agents such as quinuclidinyl benzilate. As our understanding of psychoactive drug effects has progressed over the last 50 years, the limitations of the term "psychotomimetic" have become apparent and the term is now reserved to describe states of consciousness produced by PCP or high-dose or chronic cocaine and amphetamine use. It is now widely-accepted among neuroscientists, psychopharmacologists, psychiatrists, and other medical professionals that hallucinogens do not produce a "psychotomimetic" state. Rather, the latest scientific evidence is that these compounds produce a beneficent state with sustained positive changes in attitudes and behavior (Griffiths et al., 2006; Griffiths et al., 2008). The state has been described as a mystical or religious experience, not a "psychosis" (Griffiths et al., 2006; Griffiths et al., 2008). According to reports from Daime users, this is precisely what is achieved.
20. In section II. 11. a. i., referring to Daime given to volunteers (Riba et al., 2003), Dr. Frankenheim states that "Diastolic blood pressure showed a significant increase. . ." While both diastolic and systolic pressures are important, systolic pressure, not diastolic pressure, is a stronger predictor of negative health consequences such as coronary heart disease, stroke, and end-stage renal disease (He and Whelton, 1999a; He and Whelton, 1999b). Dr. Frankenheim's statement is misleading on another level: "significant" in the context of the study refers to statistical significance, not physiological significance. The highest actual increase in diastolic blood pressure observed in this study (at one time point) was 9 mm Hg. The elevation was more typically only 3-5 mm Hg throughout the 4 hour observation period (Riba et al., 2003). These small increases in diastolic blood pressure are of absolutely no physiological consequence; notably, all of the measured pressures were within the optimal values of blood pressure as determined by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (Chobanian et al., 2003). Furthermore, no changes were observed in two other parameters (systolic blood pressure and heart rate) of greater physiological importance in the study cited. In an earlier study by the same group, no statistically or clinically relevant changes were observed in any cardiovascular parameters whatsoever (Riba et al., 2001b).
21. Dr. Frankenheim states that "it is possible to predict the toxicology of ayahuasca based on scientific evidence about its active components". However, Dr. Frankenheim makes no such prediction, later stating that a risk/benefit analysis "is not feasible at this time" because benefits have not been recognized by the FDA or the medical community at large. (Section II. 8.) This position implies that the only benefits to be considered in a risk/benefit analysis are those recognized by the FDA or medical professionals. But many drugs are legally and beneficially used outside of medical settings. Examples include the drinking of tea (containing the drug theophylline) for pleasure or relaxation, the consumption of peyote (containing the drug mescaline) for religious purposes, the consumption of beer (containing the drug alcohol) for pleasure or inebriation, etc.
22. Dr. Frankenheim states that "Generally, toxicity of drugs is determined by statistically estimating the acute dose that kills 50% of the laboratory animal subjects, the LD50 (median lethal dose)". Dr.

Frankenheim has correctly defined the classical LD50 test; however, the LD50 test is essentially an obsolete test because it is neither reliable nor particularly useful. Although the LD50 test was used in early toxicology research, it is rarely (if ever) used in modern times. Among the numerous problems (ethical, etc.) associated with the LD50 test, many problems have been identified that directly affect the test outcome itself. For example, strain differences (e.g. Sprague-Dawley rat vs. Fischer 344 rat), species differences (e.g. rat vs. human), differences in routes of administration (e.g. oral vs. intraperitoneal injection), animal housing conditions, and others factors can skew the test, making the results unreliable. For these reasons, modern toxicity testing is deemphasizing whole animal testing in general (let alone LD50 testing). Toxicity assessment is instead emphasizing other assessments such as changes in various genetic markers, not death. Modern toxicity testing approaches employ *in vitro* methods using tissues and cell lines (e.g. DNA microarray) and *in silico* methods using computer models to predict toxicity (Collings and Vaidya, 2008; Mendrick, 2008). It is significant that the FDA itself discourages the use of the LD50 test. In fact, the following organizations either strongly discourage the use of or do not use the LD50 test at all: the U.S. Consumer Product Safety Commission, U.S. Department of Transportation, U.S. Environmental Protection Agency, U.S. Food and Drug Administration, the National Toxicology Program (including the National Institute of Environmental Health Sciences of the National Institutes of Health, the National Center for Toxicological Research of the FDA, and the National Institute for Occupational Health and Safety of the Center for Disease Control), Organization for Economic Cooperation and Development, British Toxicology Society, and the European Chemical Industry Ecology and Toxicology Center (see <http://oacu.od.nih.gov/ARAC/iracl50.pdf>).

23. Dr. Frankenheim purports that Daime is toxic by citing several studies suggesting that the combination of harmala alkaloids and 5-methoxy-*N,N*-dimethyltryptamine (not DMT) can produce toxicity or death. In general, these studies are unrelated to Daime use. For example, the Balikova report (Balikova, 2002) refers to "an unusual poisoning incident" in Prague, Czech. An herbal tea (but not Daime) was consumed that resulted in numerous pathological effects including tachycardia, respiratory depression, and coma. Analysis revealed that this herbal tea contained highly toxic substances such as atropine, scopolamine, and other alkaloids found in various plants such as *Datura* species (e.g. thorn apple) and *Atropa* species (e.g. belladonna). Notably, no DMT was identified in the tea or in any of the biological samples obtained from these poisoning subjects. Two other studies cited by Dr. Frankenheim (Brush et al., 2004; Sklerov et al., 2005) concern poisoning due to the ingestion of 5-methoxy-*N,N*-dimethyltryptamine, not Daime. Again, the Frison report (Frison et al., 2008) concerns intoxication with harmala alkaloid-containing *Peganum harmala* seed extract, not Daime. Interestingly, the Gable paper cited by Frankenheim (Gable, 2007) is an attempt at risk assessment for Daime by reviewing existing scientific literature and Internet information. Dr. Gable estimates a median "safety margin" or "safety ratio" of oral DMT of approximately 21-fold. According to his calculation, the consumption of 21 ceremonial doses of Daime would be required to produce lethality in 50% of individuals. Dr. Gable goes on to say that "To this author's knowledge, there have been no deaths caused by hoasca or any other traditional DMT/b[eta] carboline ayahuasca brews. *The probability of a toxic overdose of ayahuasca is seemingly minimized by serotonin's stimulation of the vagus nerve which, in turn, induces emesis near the level of an effective ayahuasca dose.*[emphasis added] The risk of overdose appears to be related primarily to the concurrent or prior use of an additional serotonergic substance. People who have an abnormal metabolism or a compromised health status are obviously at a greater risk than the normal population, and might prudently avoid the use of ayahuasca preparations" (Gable, 2007). Tellingly, Dr. Frankenheim fails to note this latter discussion by in the Gable report, apparently because it does not support his position.


24. Frankenheim Section II. 9. c. is obvious fear-mongering and completely specious; bacteria and fungi are ubiquitous in the environment and one could say the same of any plant such as dried oregano or dried flowers.
25. Frankenheim Section II. 10. repeatedly attempts to link Daime with the unrelated drug, LSD.
26. Frankenheim Section II. 11. displays more purely speculative fear-mongering by Dr. Frankenheim as for example: "In other words, increasing the ayahuasca dose (for example, doubling it, or, for another example, "stacking" doses (i.e., taking a second dose before the effects of the first dose have completely waned)) may yield a greater-than-expected amount of DMT in the brain and greater-than-expected consequences. This is purely hypothetical. One could suggest that anyone may consume more of anything to yield a greater-than-expected consequence. Water intoxication is well-known to produce unintended fatalities.
27. Frankenheim Section II. 12. a. ii. Dr. Frankenheim states that "Though the harmala alkaloids are "reversible" inhibitors of MAO . . . their sojourn in the human body lasts much longer than that of the DMT (Riba, et.al., 2003)". This is incorrect; actually, the harmala alkaloids responsible for the bulk of MAO inhibitory activity in Daime (harmine and harmaline) return to baseline (i.e. "zero") within 6-8 hours, paralleling the presence of DMT in the human body (Yritia et al., 2002; Riba et al., 2003). Other harmala alkaloids found in Daime are only weak inhibitors of MAO (Buckholtz and Boggan, 1977).
28. MAO exists in two forms, termed MAO-A and MAO-B. The MAO enzymes metabolize many thousands of substances including the trace amine tyramine. Tyramine is a simple arylamine, namely 4-hydroxyphenethylamine. Tyramine is found in many foods including wine, beer, sherry, aged cheese, yeast extract, protein extract, soy sauce, fava or broad bean pods, smoked poultry, meats, and fish (lox, smoked salmon), pickled poultry, meats, and fish (pickled herring), chicken livers, fermented sausage (bologna, pepperoni, salami, summer sausage) and other fermented meats, bananas, avocados, and over-ripe fruit. Tyramine has the ability to release norepinephrine, leading to an increase in blood pressure and heart rate. In high amounts, tyramine can produce a potentially fatal hypertensive crisis characterized by hypertension, tachycardia, severe headache, fever, and mydriasis. Normally, MAO metabolizes and deactivates the tyramine in foods before it can be systemically absorbed, thereby avoiding the potential problems associated with too much tyramine. About 50% of tyramine is deactivated by MAO-A and the rest is metabolized by MAO-B and other metabolic enzymes (Morin et al., 2002). Earlier antidepressant drugs (e.g. tranylcypromine, phenylzine) were *nonspecific, irreversible* inhibitors of MAO; these drugs inhibit both MAO-A and MAO-B and they do so irreversibly. The MAO enzymes are permanently inactivated (at least until the cells synthesized fresh MAO), and patients taking these drugs are unable to metabolize the dangerous tyramine. For this reason, they must avoid the foods listed above.
29. The harmala alkaloids in Daime differ from the early antidepressants in that they are both *selective* and *reversible* inhibitors of MAO. The harmala alkaloids are *selective* for MAO-A, thus, MAO-B is still available to function as normal and degrade tyramine. The *reversible* aspect of the harmala alkaloids means that they do not permanently bind to and inactivate the MAO-A enzyme, as the early antidepressants do. The harmala alkaloids bind, unbind, bind, unbind, and so on in a dynamic process. When the MAO-A is in the unbound state, it is free to metabolize tyramine. Thus, if a problematic molecule such as tyramine is present, the MAO-A still has a chance to deactivate it, and the MAO-B and other tyramine-metabolizing enzymes are still available to deactivate it as well.
30. Like the harmala compounds found in Daime, the antidepressant drug moclobemide is also a *selective* and *reversible* inhibitor of the MAO-A isozyme. Significantly, moclobemide has a negligible

propensity to induce hypertensive crisis after ingestion of tyramine-rich food ("cheese-reaction") (Fulton and Benfield, 1996; Bonnet, 2003). Therefore, dietary restrictions with moclobemide are not as strict as with older, nonselective, irreversible MAO inhibitors. In fact, there is no need for patients on moclobemide to avoid dietary tyramine or over-the-counter cold remedies or decongestants containing sympathomimetic amines unless very high doses of moclobemide are taken (Fulton and Benfield, 1996; Bonnet, 2003). It is reasonable to expect that the dietary recommendations for Daime users would be similar. Nevertheless, as stated in my original declaration, it would be prudent to restrict the consumption of high-tyramine containing foods or beverages when consuming Daime.

31. Frankenheim Section II. 12. c. expresses concern that ". . .the extents to which the drugs in ayahuasca cross the placental barrier and concentrate in the fetal brain are not known. . ." This is a straw man argument; there is no "placental barrier". It is widely recognized that most drugs taken by the mother have access to the fetus (Briggs et al., 2008).
32. Frankenheim Section II. 12. f. iv. ". . . Though the classic hallucinogens are not known to produce addiction or dependence, this drug class does not consist of drugs that are all exactly alike, but rather comprises a somewhat heterogeneous group of drugs. . .which may vary in addictiveness." Section II. 12. f. v. states ". . .there is risk that ayahuasca can produce drug addiction. . ."
33. Addiction is defined by medical professionals, in the joint consensus statement of the American Society of Addiction Medicine, the American Academy of Pain Medicine, and the American Pain Society, as "a primary, chronic, neurobiologic disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterized by behaviors that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving." (see <http://www.painmed.org/pdf/definition.pdf>)
34. There are no reports in the scientific literature, or, for that matter, any anecdotal reports, that ayahuasca users engage in behaviors associated with addiction or that they fit the medical definition of addiction. Indeed, even the National Institute on Drug Abuse does not consider hallucinogens such as LSD, psilocybin, or DMT to be drugs of "addiction" because they "do not produce compulsive drug-seeking behavior, as do cocaine, amphetamine, heroin, alcohol, and nicotine" (Anonymous, 2008). Conclusion: no evidence exists to support the claim that there is a risk of addiction from Daime use.
35. Dr. Glass makes a curious statement in his declaration: " MAOIs interact with foods that contain tyramine, an essential amino acid. . ." This is incorrect; tyramine is neither an amino acid nor essential. The statement highlights a basic confusion on the part of Dr. Glass regarding human biochemistry, which in turn diminishes confidence in his other assertions. The recognized essential amino acids are in fact phenylalanine, valine, threonine, tryptophan, isoleucine, methionine, leucine, and lysine (Young, 1994). And, as already noted earlier, tyramine is 4-hydroxyphenethylamine; it does not incorporate an acid moiety.

The statements set forth in this document are my own and are based on my education and experience. Pursuant to 28 USC § 1746, I declare under penalty of perjury that the foregoing is true and correct.

DATED this 9 day of January, 2009



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Nicholas V. Cozzi, Ph.D.

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