Exhibit 2

UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF GEORGIA
ATLANTA DIVISION

UNITED STATES OF AMERICA, Plaintiff, v. Undetermined quantities of all articles of finished and in-process foods, etc. Defendants, and HI-TECH PHARMACEUTICALS, INC. and JARED WHEAT, Claimants.	Civil Action No. 1:13-cv-3675 Hon. Willis B. Hunt, Jr.

DECLARATION OF MICHAEL LUMPKIN, Ph.D, DABT

Comes now, Michael Lumpkin, and pursuant to Title 28, United States Code, Section 1746, I certify under the penalty of perjury that the contents of the following declaration are true to the best of my knowledge, information and belief:

Qualifications & Experience

1. I am a Senior Toxicologist at the Center for Toxicology and Environmental Health, LLC (CTEH®) specializing in chemical exposure and risk assessment, toxicity evaluations of chemicals, mixtures, and products. I also specialize in the evaluation of safety of dietary supplement ingredients and

products, and in experimental design and methodologies pertaining to evaluating causal relationships between chemical exposure and disease.

2. I received a Bachelor of Science (Biochemistry) degree from the University of Georgia in 1994. I received a Doctor of Philosophy degree in Toxicology from the University of Georgia in 2002. I have been certified as a Diplomate of the American Board of Toxicology since 2008. As a board-certified toxicologist, I have held memberships in multiple scientific societies, including the Society of Toxicology, the Society of Risk Analysis, and the American Industrial Hygiene Association. I have served as the President of the Southeastern Regional Chapter of the Society of Toxicology, and am currently serving as councilor for the Risk Assessment Specialty Section of the Society of Toxicology. I have been a peer reviewer for toxicological journals and federal research grant proposals. I have been an invited lecturer to graduate students in toxicology and public health at Emory University and the University of Georgia.

3. As a professional toxicologist, I have authored and published manuscripts in peer-reviewed scientific journals, and have authored textbook chapters used for training graduate-level students in toxicology and occupational health.

4. My current duties as a Senior Toxicologist at CTEH® include serving as a consulting toxicologist and expert witness in toxic tort and regulatory

litigation; providing risk assessment data analysis and interpretation; leading emergency responses to and providing toxicological support for hazardous materials release incidents; and providing on-call toxicological support to medical care providers, first responders, and workers with potential occupational chemical exposures.

5. I have evaluated and performed analyses of human and animal pharmacokinetic data for pharmaceutical products in support of New Drug Applications (NDAs) submitted to the U.S. Food and Drug Administration (FDA). Pharmacokinetic data are used to understand the extent and differences in the disposition of drug active and inactive ingredients in animal or human organ systems in non-clinical studies and clinical trials.

6. With regard to the safety assessment of dietary supplements, I have evaluated published and unpublished studies and developed data synopses for numerous individual ingredients, including 1,3-dimethylamylamine (DMAA). I have designed and monitored laboratory animal subchronic toxicity studies of dietary supplements carried out at Good Laboratory Practice (GLP)-compliant third party laboratories. I used the data from those studies and FDA-developed methodology to extrapolate toxic and safety dose levels from laboratory animals to human dietary supplement users. I have consulted with dietary supplement

producers to develop safety assessment program frameworks, and have performed risk-benefit analyses and data gap evaluations for dietary supplement ingredients.

7. Regarding DMAA, I have co-authored and presented assessments of safety and comparative effects to U.S. Department of Defense (DoD) medical and policy administrators and commanders. I have evaluated case data for individuals experiencing adverse events that occurred after the alleged use of dietary supplements, including DMAA. I have also developed assessments of DMAA safety, pharmacokinetics, and pharmacology for use by legal counsel.

8. Since 2011, I have given expert deposition testimony in a single case involving alleged adverse effects from occupational exposure to ammonia gas (Wiek v Southern Towing Company, In the United States District Court for the Western District of Tennessee, Western Division, Civil Action Number 2:13-CV-02416-JTF-tmp). I have attached a copy of my *curriculum vitae* (CV) in Exhibit A. My CV lists all of the articles that I have published within the past ten years.

MATERIALS REVIEWED

9. In preparing this declaration, I have reviewed and relied upon numerous sources of data related to dietary supplement use and safety in general and DMAA specifically, including the following:

- Published studies (pre-1950) of cardiovascular effects of DMAA in animals and human volunteers (study citations in Reference section of this Declaration) ,

- Eli Lilly's Forthane® NDA and related drug efficacy and safety data (Lilly Research Laboratories, 1980),
- Published human clinical trials of DMAA, DMAA and caffeine, and DMAA-containing products (study citations in Reference section of this Declaration),
- U.S. DoD 2013 DMAA Safety Review Panel report (Lammie, 2013)
- FDA's Center for Food Safety and Applied Nutrition (CFSAN) Adverse Effects Reporting System (CAERS) data for adverse effects potentially associated with use of DMAA-containing products (FDA 2105),
- FDA CAERS reports of vitamin C and multivitamin products (CTEH, 2015),
- Environ Corporation 2012 DMAA safety assessment (Environ, 2012a) and DMAA/caffeine comparison reports (Environ 2012b),
- FDA's 2012 press release regarding warning letters sent to DMAA-supplement manufacturers regarding dietary supplement products containing DMAA (FDA, 2012),
- FDAzilla.com records of FDA Form 483 observations (FDAzilla, 2015),
- Hi-Tech's product labels (provided by Counsel on November 3, 2015) and recommended dosage (45-90 mg DMAA/day) instructions for DMAA-containing products, including:
    - Lipo Therm
    - Yellow Scorpion
    - Black Widow
    - Lipodrene
    - Lipodrene Hardcore
    - Lipodrene XTREME
    - Fastin
    - Fastin-XR
    - Stimerex-ES/Blister Pk
    - Stimerex HC
    - Hydroxyelite
    - ECA Extreme
- Sixty three months of Hi-Tech's sales data for DMAA-containing products (Hi-Tech, 2015), and

- Case reports regarding DMAA published in the scientific literature (study citations in Reference section of this Declaration).

10. In addition to reviewing scientific literature, regulatory data, and product composition/use data, I also visited Hi-Tech's facility in Norcross, Georgia. While there, I observed product ingredient storage, manufacturing, and distribution processes. I met Mr. Jared Wheat, the owner and president of Hi-Tech Pharmaceuticals, and Samuel Dominguez, the quality control director at Hi-Tech Pharmaceuticals.

11. I also interviewed Mr. Jared Wheat and Samuel Dominguez by phone, and discussed Hi-Tech's practices regarding supply-side, midstream, and product-side material quality/purity analysis and procedures.

12. I consulted the online data intelligence service, FDAzilla, to find the rate of FDA Form 483s issued to Hi-Tech and other pharmaceutical companies. FDA Form 483s list observed deficiencies, if any, and are issued to companies by the FDA following site inspections. I found that Sanofi-Aventis U.S received 136 Form 483 observations from 249 inspections, Novartis had 137 observations from 244 inspections, and Pfizer, Inc. had 207 observations from 404 inspections. All of these 483s were issued following inspections from 2000-2015. By contrast, I found that Hi-Tech Pharmaceuticals received no Form 483s from 2001 through its last FDA inspection in November of 2013. These observations are evidence that

Hi-Tech Pharmaceuticals manufacturing sites and activities are operated to a level of care above that of major pharmaceutical companies operating in the United States.

13. A list of documents I have relied on and cited in support of my opinions is provided in Exhibit B to this declaration.

SUMMARY OF OPINIONS

14. Upon review of the data listed above, I offer the following opinions, which are given to a reasonable degree of scientific certainty:

1. Peer-reviewed published clinical trials, as a whole, show that acute (single serving) or subchronic (approximately 12 weeks) DMAA ingestion at doses at or below levels recommended on Hi-Tech product labels (≤90 mg per serving) are safe for healthy individuals, and do not indicate clinically-relevant adverse health effects.

2. A Department of Defense (2013) study of dietary supplement and DMAA use among active duty U.S. military personnel did not detect any increase in adverse health risks for military personnel using DMAA-containing dietary supplement products.

3. The negligibly small number of adverse effects reported to FDA by users of Hi-Tech DMAA-containing products compared to the number of servings sold by Hi-Tech from (2010) to (2015) suggests that DMAA consumption in dietary supplements is no riskier than consumption of other dietary supplements that are generally recognized as safe.

4. Published case reports of adverse health effects linked by the study authors with alleged DMAA consumption as a dietary supplement, individually and as a whole, are not sufficiently robust to support general or specific causation of DMAA-mediated toxicity.

5. During my visit to Hi-Tech's facility, interviews with Hi-Tech personnel, review of QC documents, and review of FDA 483 records

(or lack thereof), I did not observe any activities or processes that would lead me to conclude that the manufacture and quality of Hi-Tech's products are less than acceptable for public health.

PRINCIPLES OF TOXICOLOGY AND SAFETY ASSESSMENT

15. Toxicology is the science of identifying and quantifying adverse effects of chemical or physical agents (toxicants) on living organisms. A toxicant is any agent that can produce adverse effects on a biological system. As a general principle, any chemical or compound will produce an adverse effect on an organism if the exposure is sufficiently high. This fundamental principle of toxicology was expressed in 1538 by the Swiss renaissance physician, Paracelsus, who stated:

> *"All substances are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy".* (Klaassen, 2013)

16. Because all substances can be toxic, evaluation of exposure conditions and dose levels (i.e., exposure science) to assess safety is crucial in understanding health risk imbued by a particular substance.

17. The correlation between varying dose (or exposure) levels and the effects on a biological system is referred to as the dose-response relationship. This relationship is the most fundamental concept in toxicology and pharmacology (Klaassen, 2013).

18. The dose-response relationship is used by toxicologists to determine exposure levels that result in chemical presence in target tissues at sufficient concentrations and for a sufficient period of time to elicit an adverse effect. Similarly, when chemicals with known beneficial effects (i.e. vitamins, dietary supplements, drugs, etc.) are tested, the dose-response relationship for desired effects may be identified and compared with the adverse effect dose-response. The difference between dose-responses for the desired efficacy and undesired toxicity of a compound or mixture informs the safety of that compound or mixture.

19. Toxicology is an interdisciplinary science. Data that can be used to identify a dose-response relationship for a chemical may come from various types of investigations. Human clinical trials or volunteer experiments are conducted to evaluate the efficacy of a compound or product to elicit a desired effect and to identify potential adverse side effects. Controlled laboratory animal experiments are conducted to evaluate the toxicity and/or effectiveness of chemicals and chemical mixtures. Epidemiological studies may be used to identify associations between exposure to compounds and the onset of disease or injury for populations that are typically larger than can be reasonably observed in volunteer or early-phase clinical trials. The strength of these associations can be evaluated in epidemiological studies that reliably differentiate populations who experience differences in exposure levels, exposure durations, or both.

20. Evaluations of a substance's safety and toxicity typically consider a range of dose concentrations to determine the continuum of pharmacological/toxicological responses. Some of the most important points along this dose continuum include the No Observed Adverse Effects Level (NOAEL), which is the highest dose tested that does not elicit an adverse effect, and the Lowest Observed Adverse Effects Level (LOAEL), the lowest dose tested that elicits an adverse effect. Similarly, the Effective Dose is the dose at which 50% of a population exhibits the desired effect (ED_{50}) for a physiologically-active dietary supplement. **Figure 1** illustrates these concepts, and shows how an ingredient such as one found in a dietary supplement is able to elicit a desirable effect at doses below which no adverse or toxic effects are observed.

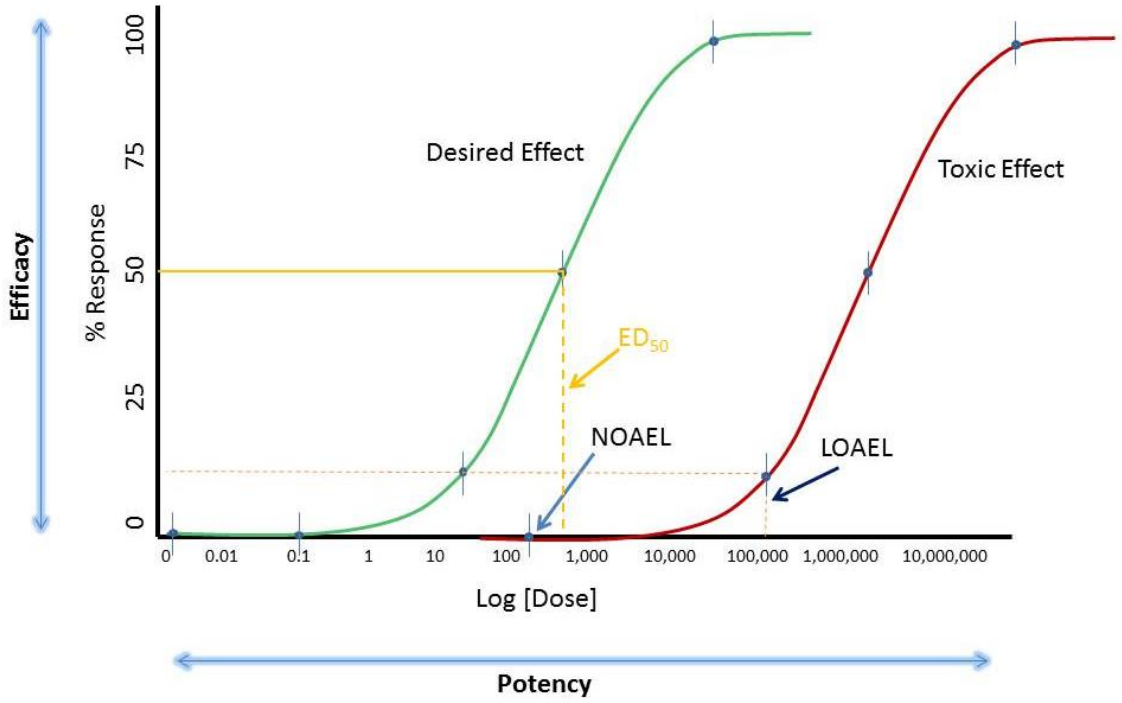

Figure 1. Dose-Response Relationship Curve

An important distinction should be made between a dose level that results in adverse effects that are subjective in nature (i.e., headache, jitteriness, nausea) and toxicity. In toxicology, toxicity is defined as the effect, possibly reversible, of a compound on a tissue or organ system that results in the inability of the tissue or organ system to perform its normal function. Subjective health complaints are not typically deemed toxic effects unless a clinically-apparent adverse change can be identified. Thus, all toxic effects are adverse effects, but not all adverse effects are toxic effects.

OVERVIEW OF DMAA

21. DMAA is an aliphatic amine that acts as a sympathomimetic molecule in mammals. It is also known as 1,3-dimethylamylamine, methylhexamine, methylhexanamine, methyl hexane amine, 1,3-dimethylpentylamine, pentylamine, 2-hexanamine, 2-amino 4-methyl hexane and other names. A sympathomimetic compound is a chemical that mimics some of the body's naturally-formed compounds (i.e., catecholamines like epinephrine) that, themselves, act on the sympathetic nervous system. The sympathetic nervous system is a part of the nervous system that regulates the unconscious functions of organs involved with the "fight-or-flight" response.

22. DMAA was patented by Eli Lilly in 1944. It was approved by the FDA in 1948 for use as an over-the-counter nasal decongestant marketed as Forthane®. The Forthane product delivered a nasal spray dose of 250 mg DMAA. Its ability to induce vasoconstriction and reduce swelling of the nasal tissue, similar to ephedrine and amphetamine, but without potent central nervous system (CNS) side effects, made it an attractive molecule as a decongestant (US Patent Office, 1944 as cited in Rodricks et al. 2012). Forthane® production was discontinued in 1983 (FDA, 1983) for market reasons, not for reasons of adverse health effects.

23. There is an ongoing debate in the peer-reviewed scientific literature as to whether or not DMAA occurs naturally in plants (Ping et al., 1996; Li et al., 2012; Fleming et al., 2012; Gauthier 2012, 2013; Zhang et al., 2012; ElSohly et al., 2012; Lisi et al., 2011). Regardless of source, the biological, pharmacological, and toxicological effects of any naturally- and synthetically-derived chemical are the same. The identical chemical structure of natural or synthesized DMAA means that natural or synthetic DMAA will behave identically in the body, making the DMAA source an irrelevant aspect to the assessment of safety.

24. Like other sympathomimetic compounds, DMAA can mimic the effect of neuro-active catecholamines produced within the body, such as epinephrine and norepinephrine (**Figure 2**).

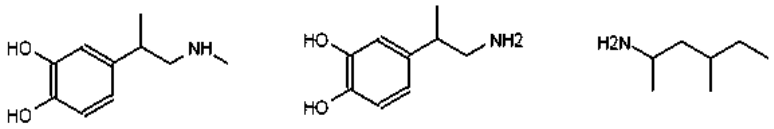

Figure 2. Chemical structure of epinephrine (left), norepinephrine (center), and DMAA (right)

25. DMAA has been shown to have vasoconstrictor effects like epinephrine, but at doses approximately 200-times higher than those at which epinephrine elicits vasoconstriction of equal intensity when administered intravenously (Marsh et al., 1951). Additionally, intravenous injection studies have shown additional, short-lived sympathomimetic effects of DMAA on blood pressure and heart rate (Chen, 1948, Beyer, 1946), whereas topical administration studies show little or no effect on heart rate or blood pressure in adult humans.

26. The ability to induce sympathetic responses is shared among these molecules. Ephedrine, pseudoephedrine, norepinephrine and other catecholamines induce a sympathetic nervous system response by directly stimulating adrenergic receptors - molecules on nerve cells that elicit a response when they are bound by a sympathomimetic compound. However, DMAA likely induces a sympathetic response through indirect mechanisms, such as the inhibition of reuptake (and thus, accumulation) of norepinephrine in the gaps between nerve cells where nerve

signals are transmitted. This is consistent with mechanisms of action shared by its structural cousin, 2-amino heptane, although its exact mechanism of action remains incompletely understood (Delicado et al., 1990). To the best of my knowledge, no studies have reported DMAA or 2-amino heptane acting as direct sympathomimetics.

27. This characteristic difference in action between aliphatic amines like DMAA and catecholamine-like molecules such as epinephrine and ephedrine was addressed by Barger and Dale (1910), who stated that the catechol nucleus (ringed carbon substituent) in the epinephrine molecule caused a rise in blood pressure when injected intravenously, while methyl-amino-ethanol, which does not have a catechol nucleus, has no such action. They further stated that the similar increase in blood pressure attributed to certain amines lacking a catechol nucleus was due to an action of an entirely different type than for the catechol-like compounds.

28. DMAA has been referred to as an "amphetamine derivative" by the FDA (FDA 2013), while others compare its sympathomimetic action (acting in the sympathetic nervous system) to that of amphetamines or amphetamine-like substances such as ephedrine (Cohen, 2012; Gee et al., 2012).

29. However, a significant difference exists between DMAA and amphetamine-like substances in the structural chemistry that results in significant differences in pharmacological action.

30. Amphetamine is chemically synthesized by the reduction of 1-phenyl-2-propanone (P2P) by reacting formamide with P2P in the presence of formic acid (HSDB, 2015). DMAA may be synthesized by reacting 4-methyl-2-hexanone with hydroxylamine, formamide, ammonium formate, or ammonia and hydrogen (in the presence of a catalyst, such as Rainey nickel) (U.S. Patent Office 1944 as cited in Rodricks et al. 2012). DMAA is not synthesized from precursors containing conjugated benzene rings (i.e., P2P or amphetamine), but from an aliphatic ketone (4-methyl-2-hexanone). Thus, DMAA is not an amphetamine derivative, nor is it in the same chemical class as amphetamine.

31. DMAA contains a carbon backbone and an aminomethyl (NH_2-CH_3) end. Amphetamine (1-phenyl-2-aminopropane) is in the phenethylamine class, an organic compound having both a phenyl group (benzene ring) and an aminomethyl (NH2-C-CH3) group (**Figure 3**). The absence of a benzene ring in DMAA significantly affects the way the compound interacts with molecular components (i.e., receptors) in neurons. This structural feature is required for perturbation of the neurotransmitter release and re-uptake in the dopaminergic or adrenergic neurons (Biel and Bopp 1978). Since it does not possess a benzene ring, DMAA is unlikely to produce these effects.

Figure 3. Comparative chemical structures of DMAA (left) amphetamine (right)

32. The concentration of DMAA over time in blood plasma was measured in adult males who consumed 25mg DMAA (Schilling et al., 2013). In this study, DMAA was detected in the blood at approximately 8 minutes, with peak average concentrations of approximately 77 ng/ml of plasma occurring at 3-5 hours after dosing. The terminal half-life (time point during elimination from the blood that the DMAA concentration fell to ½ of the maximum concentration) was approximately 8.5 hours.

33. A study was published by Liu and Santillo (2015) in which the study authors investigated the ability of several dietary supplement stimulant compounds, including DMAA, to inhibit specific liver enzymes, named CYP3A4 and CYP2D6. These enzymes are known to metabolize many therapeutic drugs. The study was not conducted in humans, animals, isolated tissues, or even intact cells, but in a commercially-available laboratory assay (i.e., *in vitro*) kit. Solutions of purified CYP3A4 and CYP2D6 liver enzymes were incubated in a laboratory container with varying concentrations of single stimulants, and the extent to which the stimulant inhibited, or blocked, the enzymes' ability to metabolize other compounds was measured. The study authors reported that DMAA was one of a

group of compounds that caused less than a 15% inhibition of CYP3A4 when present at a concentration of 100 micromolar (µM). Further, the DMAA concentration in the CYP2D6-containing solution that caused a 50% inhibition (IC_{50}) of CYP2D6 was 6.5 µM.

34. In isolation, these data (Liu and Satillo, 2015) for DMAA are meaningless regarding safety. They may be used for comparison with inhibition data for other compounds to determine relative inhibitory potency among the studied stimulants. In that role, the data may be used to identify and target the more potent inhibitory compounds for further research utilizing intact humans or animal (i.e., *in* vivo) studies. However, knowing the inhibitory concentration of DMAA in a cell-free environment alone does not at all inform how it might affect the ability of liver enzymes to properly metabolize therapeutic drugs.

35. It is important to understand context in which the Liu and Satillo (2015) *in vitro* data were generated. The concentration of DMAA in a plastic or glass laboratory container with fluid containing liver enzymes may never actually occur in an intact liver of a human or animal. The concentration of DMAA in any ingested food, drug, or dietary supplement may be different from the concentration of DMAA that is absorbed from the gut to the blood. The DMAA concentration in the blood may differ markedly from that within the liver tissues. Liver tissue DMAA levels may differ from levels in liver cells, and biochemically-active

compounds and processes within a cell may significantly impact the amount of DMAA that may interact with CYP3A4 and CYP2D6. Thus, there are multiple levels of physiological complexity (whole body, blood, organ, cell, and enzyme microenvironment) through which DMAA must pass to impact specific biochemistry such as effects on CYP3A4 and CYP 2D6.

36. There is a useful comparison to be made of the Liu and Satillo (2015) *in vitro* data with the Schilling et al. (2013) *in vivo* human data described previously in paragraph 32 of this declaration. The Liu and Satillo (2015) DMAA IC_{50} for CYP3A4 is 6.5 µM, or 748 ng/ml (based on a DMAA molecular weight of 115) of enzyme-containing solution. The peak blood DMAA plasma concentration in volunteers ingesting 25 mg DMAA was reported by Schilling et al. (2013) to be 77 ng/ml. Thus, if the DMAA level in the liver cells were roughly equal to that of the blood plasma DMAA levels of persons consuming 25 mg DMAA, and the body did not respond to DMAA presence with some compensatory biochemical mechanism, then the liver cell DMAA level would still by approximately 10-times lower than the level shown by Liu and Satillo (2015) to significantly inhibit CYP3A4 or CYP2D6 metabolic activity.

SAFETY OF DMAA

37. I have reviewed the scientific literature containing data relevant to the safety of DMAA, both as a single compound and as a constituent of dietary

supplements. This section of my declaration includes a summary of animal and human data that I deemed relevant to answering the following general causation question: Can consumption of DMAA at levels recommended or suggested by the labeling of Hi-Tech products cause adverse health outcomes and death?

Animal Studies

38. I identified studies published in the 1940's and 1950's in which the pharmacological activity and toxicity of aliphatic amines such as DMAA were evaluated and compared with the same endpoints for amphetamine, ephedrine and other aromatic amines. Marsh et al. (1951) reported that 0.7 DMAA per kg of body weight (mg/kg) resulted in increased pressor activity (blood pressure), which was 189-times lower than an equivalent active dose of epinephrine. Swanson and Chen (1946) showed that, while DMAA had greater pressor (increase in blood pressure) activity than 38 other aliphatic amines when injected in dogs (Swanson and Chen, 1946), it also had the weakest pressor action when administered orally, stating:

> "*only in large doses was there evidence of absorption of 2-amino-heptane and 2-amino-4-methyl-hexane [DMAA], as measured by the rise in blood pressure".*

39. In fact, the fraction of absorbed DMAA was calculated by the study authors to be 25% of ephedrine absorption, and 50% of amphetamine doses (Swanson and Chen, 1948). This observation highlights the fact that, non-orally

administered doses do not necessarily reflect the pharmacological or toxicological effects that may result from oral consumption of equivalent doses, on a body weight basis. For example, while an intravenous dose of 0.26 mg mg/kg in cats and dogs was sufficient to elicit an increase in blood pressure, oral doses of 5 to 20 mg/kg (20 to 100 times higher than those from intravenous administration) were necessary to elicit a comparable increase in blood pressure (Swanson, as cited in Eli Lilly NDA 6-4444, 1980; Swanson and Chen, 1946; Swanson and Chen, 1948).

40. Two animal studies conducted by Clintox Bioservices (2012a, 2012b) evaluated body weight, feed intake, mortality, gross pathology, and clinical observations such as tremor, convulsion, and salivation in rabbits (n=24) and Winstar rats (n=40). Animals were administered single oral doses of vehicle control (containing no DMAA), or varying doses of DMAA in the vehicle solution. Rabbits received 0, 50, 150 or 300 mg of DMAA per kg (6 animals per dose group). Rats received 0, 50, 125 or 250 mg of DMAA per kg (10 animals per dose group).

41. In the rabbit study (Clintox Bioservices, 2012a), the animals administered 300 mg/kg exhibited salivation, convulsion, and tachycardia (rapid heart rate), with four deaths occurring prior to study termination. Tremors were observed in several rabbits in the 150 mg/kg group, while no other adverse clinical observations were reported. Similarly, the groups exposed to 50 and 0 mg/kg did

not exhibit any changes in behavior or health, leading the study authors to conclude that the maximum tolerated oral dose of DMAA in rabbits was between 150 and 300 mg/kg.

42. In the rat study (Clintox Bioservices, 2012b), one pre-terminal death occurred in the 250 mg/kg group, while other animals in this group exhibited tremors. No adverse health outcomes or other clinical observations were reported for the groups treated with 0, 50 or 125 mg/kg, leading the study authors to conclude that that the maximum tolerated oral dose of DMAA in rats was between 125 and 250 mg/kg.

Overview of Human Studies Containing Safety Data for DMAA

43. Several human clinical trials have been published containing data for the consumption of DMAA and the development, or lack thereof, of adverse health outcomes. In particular, eight human clinical studies reporting health effects from DMAA and caffeine, and from products that contain DMAA, among other ingredients, (i.e. USPLabs' Jack3d™, and OxyElite Pro™), have been performed by researchers at the University of Memphis, published in peer-reviewed scientific literature, and are summarized below. These studies reported daily DMAA dose levels of approximately 0.6-1.0 mg DMAA/kg and exposure durations ranging from single doses to 2, 8, 10, and 12 weeks. The hemodynamic (blood pressure characteristic) effects reported in these studies published in the last few years

comport with effects reported in the older literature, where oral ingestion of 3 mg/kg DMAA in adult male volunteers resulted in a transient increase in systolic blood pressure beginning at about 30 minutes and decreasing after 100 minutes (Marsh et al., 1951).

44. Bloomer et al. (2011a) investigated the ingestion of DMAA and caffeine on resting hemodynamic properties and endogenous sympathetic catecholamine (epinephrine and norepinephrine) levels of volunteers for up to 2 hours after dosing. Five male and five female healthy adults consumed a single dose of 250 mg caffeine (2.8-3.4 mg caffeine/kg), 50 mg DMAA (0.6-0.7 mg DMAA/kg), 75 mg DMAA (0.9-1.0 mg DMAA/kg), or combinations of 250 mg caffeine plus 50 or 75 mg DMAA. Heart rate, diastolic blood pressure, and plasma levels of epinephrine or norepinephrine were not significantly different across all treatment groups or from pre-ingestion (control) values. After 60 minutes, systolic blood pressure was increased in all treated groups (122-143 mm Hg in a dose-related manner) above pre-ingestion values (117-121 mmHg), with 75 mg DMAA or 75 mg DMAA/250 mg caffeine producing higher values (132 and 141 mmHg, respectively) than caffeine alone (122 mmHg) at 90-120 minutes. Likewise, diastolic pressure in all treated groups (76-83 mmHg) was higher than pre-ingestion values (68-71 mmHg) after 60 minutes, but combining DMAA with caffeine resulted in values similar to caffeine alone.

45. Bloomer et al. (2011b) administered caffeine, DMAA, or combinations of both to volunteers prior to them running 10 km. Six males and 6 females with an average age of 22 years were given 0, 4 mg caffeine/kg, 1 mg DMAA/kg, or a combination of 4 mg caffeine/kg and 1 mg DMAA/kg, in 500 ml water. Treatments were ingested one hour prior to running 10 km on an outdoor track. Each subject completed four test runs with a different treatment before each run, with one week in between each test. There were no statistically significant differences between groups in required run time, perceived exertion, self-reporting of mood and vigor, and heart rate during the run. At 5 and 30 minutes post-exercise, the heart rate in the caffeine+DMAA group was higher than the caffeine or DMAA groups, but not the placebo group. Systolic blood pressure in the caffeine+DMAA group at 5 and 30 minutes post-exercise (126 mmHg) was similar to placebo (126 mmHg), but lower than the caffeine-alone (141 mmHg) or DMAA-alone (147 mmHg) groups. Diastolic blood pressure at 5 minutes post-exercise was similar across groups (64-66 mmHg), but lower in the DMAA+caffeine group (61 mmHg). The rate pressure product (a metric of cardiac workload found by multiplying heart rate and systolic blood pressure) was similar in the placebo and DMAA+caffeine groups at 5 and 30 minutes post-exercise, but higher in the caffeine-alone or DMAA-alone groups. These data indicate that a combination of 1 mg DMAA/kg and 4 mg caffeine/kg did not significantly change

physical performance, level of exertion, subject mood or vigor, heart rate, or blood pressure endpoints, compared to placebo, following a very strenuous physical activity. In addition, these findings demonstrate that some of the observed increases in heart rate and blood pressure from consumption of DMAA-containing supplements that also have caffeine may in fact be largely dependent on the caffeine content.

46. McCarthy et al. (2012a) examined the effect of single doses of the DMAA-containing dietary supplement product OxyElite Pro™ (USPLabs, LLC) on hemodynamics of healthy adults for up to two hours after treatment. Six males and 6 females were administered two capsules of OxyElite Pro™ (0.5-0.6 mg DMAA/kg and 2.5-3.2 mg caffeine/kg) or placebo on two separate days in a cross-over study design. An increase in heart rate of 8-11 beats/min (bpm) was reported in the treated group beginning at 60 minutes. Systolic blood pressure increased (112-118 mmHg) in the treated groups, compared to placebo (101-104 mmHg) beginning at 30 minutes after dosing. There was no increase in diastolic pressure.

47. Farney et al. (2012) investigated hemodynamic, hematological, and clinical chemistry effects of DMAA-containing Jack3d™ after single and 14-day dosing. Seven healthy adult males consumed DMAA and caffeine doses of 0.5 and 3 mg/kg/day, respectively. After dosing on days 1 and 14 (acute-phase observations), systolic blood pressure increased (122-123 mmHg) over pre-

ingestion values (109 mmHg) beginning at 30 minutes. There were no significant differences in acute changes in heart rate, diastolic pressure, or rate pressure product on days 1 or 14. After 14 days of dosing, no significant changes in hemodynamic endpoints compared to day 1 were reported.

48. Farney et al. (2012) also reported hemodynamic, hematological, and clinical chemistry effects of OxyElite Pro™ after single and 14-day dosing. Four healthy adult males and two females consumed DMAA and caffeine doses of 0.6 and 3 mg/kg, respectively. After dosing on day 1, systolic blood pressure increased (116-119 mmHg) over pre-ingestion values (103 mmHg) beginning at 60 minutes. There were no significant differences in acute changes in systolic pressure on day 14, or in heart rate, diastolic pressure, or rate pressure product on days 1 or 14. After 14 days of dosing, no significant changes in hemodynamic endpoints compared to day 1 were reported.

49. McCarthy et al. (2012b) examined the effect of an 8-week exposure of OxyElite Pro™ on hemodynamic, hematological, and clinical chemistry endpoints. Groups of 16 healthy, adult males and females consumed 1-2 capsules OxyElite Pro™ or two placebo capsules daily for 8 weeks, resulting in daily DMAA and caffeine doses of 0.3-0.5 and 1.3-2.6 mg/kg, respectively. In the treated group, resting heart rate was slightly, but statistically significantly, higher (69.4 bpm) at the end of the study compared to the beginning (63.3 bpm), but were not different

from the placebo control values (65-67 bpm). There were no differences between treatment groups or pre- or post-study values for systolic or diastolic blood pressure.

50. Whitehead et al. (2012) examined the effect of a 10-week exposure of Jack3d™ on hemodynamic, hematological, and clinical chemistry endpoints. Groups of 12 or 13 healthy, adult males consumed DMAA and caffeine exposure ranges of 0.3-0.8 and 1.6-4.9 mg/kg. Ten weeks of Jack3d™ use resulted in reported heart rate and systolic and diastolic blood pressure values similar to placebo controls.

51. Schilling et al. (2013) reported the blood DMAA concentration and elimination profile in 8 male adults who consumed 25 mg of DMAA in capsules. The study authors also measured heart rate, blood pressure, and body temperature over a 12-hour period post-dosing and again at 24 hours post-dosing. The average maximum plasma DMAA concentration, 67µg/L, was observed 5 hours after DMAA consumption. There was no meaningful effect on body temperature, pulse rate, or blood pressure.

52. Bloomer et al. (2013) performed a 12-week placebo-controlled safety and efficacy study in healthy male volunteers. This study is the largest and longest dietary supplement intervention study to date for both group size and treatment duration. Groups of 15 adult males consumed capsules each day containing a

placebo, 50 mg DMAA, 250 mg caffeine, or 50 mg DMAA + 250 mg caffeine. Prior to the first dose and at 6 and 12 weeks, the subjects were evaluated for hemodynamic parameters, clinical chemistry, hematology, urinalysis, blood markers for oxidative stress, inflammation, and cardiac muscle damage, and electrocardiography. No adverse changes were reported for any of the measured parameters of heart, liver, kidney, or vascular health.

53. The Bloomer group's clinical studies for DMAA and DMAA-containing dietary supplements contain similar findings for the hemodynamic effect of orally-administered DMAA alone or with caffeine: a temporary and short-lived increase in systolic blood pressure of approximately 12-18% occurring approximately 60-90 minutes after ingestion. Extended exposure exposures of 2 to 10 weeks, either daily or on workout days only, did not result in consumption duration-related increases in resting heart rate or blood pressure. A 12-18% increase in systolic pressure, 10-15% increase in diastolic pressure (in one study, Bloomer et al., 2011a), and 6% increase in heart rate in one study (McCarthy et al., 2012a) in healthy adults for periods of 1-2 hours per day is not an adverse health effect. In fact, the transient blood pressure increases are similar to those experienced during physical exercise. The temporary increases in blood pressure from DMAA and caffeine use or physical exercise are not additive, as no increase in blood pressure was reported after a 10 km run by runners who consumed

DMAA and caffeine beforehand (Bloomer et al. 2011b). These transient effects on blood pressure are not expected to have long-term adverse consequences on cardiac health, as indicated by the nominal values for cardiac health parameters reported by Bloomer et al. (2013) for a 12-week exposure duration.

54. The results of the hematological, metabolic, and lipid panel tests in the 2- to 12-week studies indicate that DMAA-containing dietary supplement use over an extended period of time does not adversely impact liver or kidney function. Self-reporting of no incidents of discomfort or elevated body temperature during an extended strenuous physical activity (10 km run) or after 12 weeks of episodic workouts does not indicate that DMAA consumption increases the susceptibility to induction of hyperthermia in healthy adults.

55. Other studies, such as those conducted by Marsh et al., (1951) have shown that individuals exposed to 3 mg/kg (more than double the maximum recommended dose of DMAA in Hi-Tech's products) present similar increases in systolic blood pressure with lesser effects on heart rate and diastolic blood pressure. The volunteer individuals were also reported to have no indication of serious adverse health effects (Marsh et al., 1951).

56. Lastly, studies of oral DMAA administration conducted in the 1940s and 1950s with small sample groups also reported findings consistent with the previously reported effects. A group of 3 individuals were given 100 mg oral doses

of DMAA, which resulted in increases in systolic blood pressure ranging between 14 and 32 mmHg, and diastolic blood pressure increases between 9 and 32 mmHg above baseline with variable changes in heart rate. Interestingly, when an additional group (n=5) were given oral doses of 25, 50, or 75 mg of DMAA, no changes in blood pressure, heart rate or experienced symptoms were observed, strongly indicating that adverse health outcomes may only be observed when given oral doses in excess of 100 mg of DMAA (Swanson et al,. as cited in Eli Lilly NDA 6-4444, 1980).

DoD DMAA Safety Review Panel Report

57. In June of 2013, the Department of Defense DMAA Safety Review Panel issued a report of a safety assessment of DMAA use among active duty military personnel (Lammie, 2013). The series of studies described in the assessment report were conducted by 27 military and civilian medical, health science, and project support personnel.

58. The DoD (Lammie, 2013) DMAA safety assessment among other things, included (a) a review of military decedent autopsy and clinical toxicology data by experts in the Armed Forces Medical Examiners System, and (b) a case-control epidemiology study of military personnel.

59. As part of the DoD safety assessment, the U.S. Armed Forces Medical Examiners identified 71 mortality cases in which physical exercise, heat stroke,

stroke, heart attack, or liver failure were involved, as well as possible DMAA-containing product use. Blood and urine samples from these cases were re-analyzed using a sensitive analytical chemistry method. Samples from 4 of the 71 cases were found to have measurable levels of DMAA present. However, the levels were extremely low, being 4-times to 100-times lower than DMAA blood levels reported by Gee et al. (2012) for deaths that those study authors attributed to recreational DMAA use (described below). The DoD study authors determined that the low DMAA blood levels in these four cases suggested that DMAA was unlikely to have played a role in death.

60. Also as part of the DoD safety assessment, U.S. Army Public Health Command designed and performed a case-control epidemiological study to investigate a possible association between DMAA use in U.S. military personnel and adverse health effects.

61. In the design of a typical case-control study, a group of individuals having experienced a specific disease or injury (or set of related diseases/injuries), the "cases," are identified. A group from the same or similar population that did not experience the disease/injury of cases are also identified. These are the "controls." The larger the groups of cases and controls, the more power that investigators using statistical analyses have to tease out confounding factors and

determine whether a specific factor may actually be linked with the disease/injuries of interest.

62. In case-control studies, a positive statistical association between a substance exposure or behavior and injury in the cases group suggests that that exposure or behavior *may*, but not necessarily, play a role in injury. Additional data from other sources, such as adverse events databases, and safety, toxicology, and other epidemiology studies, are required to establish a scientifically-strong causal link between exposure and effect (Green et al., 2011).

63. The DoD investigators identified case criteria as individuals who were diagnosed and treated in 2011 with one or more of the following injuries: heat injury, cardiac dysrhythmia, seizure, rhabdomyolysis, cerebral hemorrhage, liver necrosis, or kidney failure. Questionnaires were delivered to a group of 6,881 U.S. Army soldiers identified as cases or controls. The investigators received back completed questionnaires from 712 cases and 1,077 controls. This case-control study represents the largest population for which scientific analysis has been performed to investigate a possible association between DMAA use as a dietary supplement and specific adverse health events.

64. The statistical analysis of the case-control data showed no significant association between DMAA use and adverse health events in general or for specific injuries. In fact, the controls were found to be more likely to use DMAA

than the cases. The investigators also found that cases were less likely than controls to exercise and more likely to have a history of reporting multiple adverse events, be former smokers, and be currently taking a prescription antidepressant.

65. In spite of findings of no significant association of DMAA use with adverse health effects in military personnel, the DoD DMAA Safety Review Panel offered opinions in the Executive Summary that are not based on the data collected and analyzed by the Panel. In the Executive Summary, the Panel made the statement "*The existing evidence does not conclusively establish that DMAA-containing substances are causally-associated with adverse medical effects.*" However, the Panel then stated that "*Widespread use of DMAA-containing products by tens of thousands of Service members…increases the likelihood of observing serious adverse events*." This statement is completely without a scientific basis. It is not at all clear why the Panel would make such a statement about risk when the data that was reviewed, including published studies in human volunteers, and the Panel's own assessment found NO evidence for increased risk of serious adverse effects. However, one of the Safety Panelists, Dr. Patricia Deuster, has since opined that some supplements, including DMAA, have been *"…found to be potentially high risk…*" without providing quantitative data to back that opinion (Deuster and Lieberman, 2015).

66. The DoD assessment Executive Summary also states that "*The Panel judged that the evidence supports sufficient risk, even if very low, of another death or catastrophic illness of a Service member who has used DMAA-containing products, without any offsetting benefit of these products*." This statement is incorrect on two counts. First, the Panel did not scientifically demonstrate any increase in health risk. Second, it did not report on any consideration whatsoever of "offsetting benefit."

67. Although these statements by the Panel are solely policy-based, and not science-based, they have been misinterpreted by many in the lay literature. Articles published in Stars and Stripes (Tritten, 2013), NutraIngredients USA (Schultz, 2013), and USA Today (Kime, 2015), all discuss the DoD Panel's concern for DMAA-related health risks, as expressed in its Executive Summary, but not supported in the body of the assessment.

CARDIOVASCULAR AND THERMOREGUALTORY EFFECT INDICATORS IN THE HUMAN VOLUNTEER DATA

68. The published case reports and CAERSreports for adverse events primarily note cardiovascular and thermoregulatory (maintenance of proper internal body temperature) events after DMAA consumption. In particular, the U.S. Army had concerns arising from reports of "kidney and liver failure, seizures, loss of consciousness, heat injury and muscle breakdown during exertion, and

rapid heartbeat" among users of DMAA (Stars and Stripes 2011). An important issue to resolve is whether DMAA use, with or without caffeine, imparts significant additional risk of causing these effects. The clinical data for DMAA alone, with caffeine, and as an ingredient in dietary supplement products, indicate that, not only have these effects not been observed in the published clinical trials, but clinical precursors leading to each of the adverse effects of concern have not been observed.

69. **Loss of consciousness (syncope)**: None of the study subjects ingesting DMAA-containing dietary supplements at labeled doses reported light-headedness or loss of consciousness during or after a 10 km run (Bloomer et al. 2011b) or while using a DMAA product for up to 12 weeks in conjunction with a frequent exercise workout regimen (Bloomer et al., 2011a; Farney et al. 2012; McCarthy et al. 2012a; McCarthy et al. 2012b; Whitehead et al. 2012; Bloomer et al., 2013). Hemodynamic data from all 7 clinical studies of DMAA never indicate conditions of blood pressure drop that could have caused a diminution of conscious faculties.

70. **Heat injury (hyperthermia)**: A chemically-induced increase in risk of exertional hyperthermia requires interference with the ability of the body to shed excess heat. This interference may be caused by dehydration, significant decrease in electrolyte concentrations, and/or inhibition of sweat gland function leading to

loss of evaporative cooling at the skin surface (Armstrong et al. 2007a). No data were available to demonstrate the effect of DMAA or other aliphatic amines on diuresis, but epinephrine and norepinephrine (more potent sympathomimetics than DMAA) do not increase diuresis (Billewicz-Stankiewicz et al. 1980).

71. Healthy adults administered single exposures of DMAA plus caffeine or a DMAA-containing dietary supplement, either resting (Bloomer et al. 2011a; McCarthy et al. 2012 a, 2012b), prior to running 10 km (Bloomer et al. 2011b), or over 12-weeks (Bloomer et al., 2013), did not report an increase in subjective indicators of thirst, uncharacteristically profuse sweating, or urinary urge. In a study of healthy adults using DMAA prior to running 10 km in ambient air temperatures ranging from 44°F to 68°F, there was no indication from study subjects of thermal discomfort or change in required exertion level, compared to an identical run performed by the same subjects after consuming a placebo (Bloomer et al. 2011b). These findings from subjects performing very strenuous physical exercise at relatively mild ambient temperatures are useful in that significant changes to body heat regulation would be detected and reported without confounding by high ambient air temperatures. Similarly, subjects using DMAA-containing dietary supplements prior to exercise workout for 2 to 12 weeks did not report thermal discomfort (Farney et al. 2012; McCarthy et al. 2012b; Whitehead et al. 2012; Bloomer et al., 2013). Blood clinical chemistry results from the same

subjects did not indicate any effect on electrolyte concentrations that could be magnified if exercising in conditions of extreme heat. Thus, clinical data indicate that DMAA consumption at labeled doses of DMAA-containing dietary supplements would not increase the risk of heat injury for a healthy adult performing strenuous physical activity in hot conditions.

72. **Exertion-induced muscle breakdown (rhabdomyolysis)**: Clinical manifestation of exertional rhabdomyolysis may include muscle pain, swelling, and weakness, electrolyte imbalance, decreased renal function, abnormal heart rate, confusion, and gastrointestinal distress. None of these signs, symptoms, or indications from clinical chemistry or metabolic panel results from users of dietary supplements were reported in the six clinical studies of DMAA. Thus, use of DMAA at approximately 50 mg/day is unlikely to increase the risk for developing acute or chronic exertional rhabdomyolysis in healthy adults.

73. **Rapid heartbeat (tachycardia)**: Heart rate data from the seven clinical studies of DMAA do not indicate the occurrence of rapid heartbeat/tachycardia (Farney et al. 2012; McCarthy et al. 2012a; Whitehead et al. 2012; Bloomer et al., 2011a; Bloomer et al., 2011b; Bloomer et al., 2013), even in subjects using DMAA and caffeine prior to a 10 km run (Bloomer et al., 2011b).

74. **Liver failure**: Blood samples subjected to metabolic panel examinations were reported for subjects using DMAA-containing dietary

supplements for 2 to 12 weeks (McCarthy et al, 2012b; Farney et al. 2012; Whitehead et al. 2012; Bloomer et al., 2013). Indications of liver health included blood levels of bilirubin, alkaline phosphatase, aspartate and alanine transaminases, and gamma glutamyl transferase. In all of the multi-dose studies, these parameters were all well within clinical reference ranges, indicating the lack of evidence for subclinical precursors to liver injury or failure.

75. **Kidney failure**: Blood samples subjected to metabolic panel examinations were reported for subjects using DMAA-containing dietary supplements or DMAA alone or with 250 mg caffeine for 2 to 10 weeks (McCarthy et al, 2012b; Farney et al. 2012; Whitehead et al. 2012; Bloomer et al., 2013). Indications of kidney health included blood levels of glucose, blood urea nitrogen (BUN), creatinine, sodium, potassium, and albumin. In all of the multi-dose studies, these parameters were all well within clinical reference ranges. Thus, there was no indication of evidence for subclinical precursors to kidney injury or failure.

SCIENTIFIC DISEASE CAUSATION METHODOLOGY

76. While the FDA has not explicitly claimed that the deaths and adverse effects of specific individuals were caused by consumption of DMAA-containing products, the warning letters that they issued to manufacturers to cease distribution of DMAA-containing products and their allegation that DMAA is unsafe (FDA,

2013) are based on the assumption that DMAA was, in fact, the cause of the adverse health outcomes listed in the FDA MedWatch database, as well as those described in several published case reports (Archer et al., 2015; Armstrong 2012; Eliason et al., 2012; Foley et al., 2014; Gee et al., 2010; 2012; Karnatovskaia et al., 2015; Salinger et al., 2011; Smith et al., 2014; Young et al., 2012).

77. Established and generally accepted methods exist for determining whether an individual's disease or adverse health effects were caused by an alleged chemical exposure (i.e. through oral consumption). In order to establish that a chemical exposure can and did result in an adverse health condition, general and specific causation must be evaluated.

78. **General causation** is the scientific determination as to whether or not the chemical in question is capable of causing a particular effect in the general population at some specified dose. It is a determination of what toxicities the chemical may produce in humans.

79. **Specific causation** is a scientific determination as to whether a specific individual's or population's known or alleged chemical exposure was the most likely cause of the alleged injuries or disease.

80. The methodology for establishing general causation, as currently practiced, is a process that has undergone continual refinement for approximately the last 150 years. At the present time, a number of different criteria have been

proposed by scientists as the basis of the scientific method for establishing general causation (Hill, 1965; Evans, 1976; Hackney and Linn, 1979; Doll, 1984; Guidotti and Goldsmith, 1986; Susser, 1977, 1986, 1991). The criteria for general causation as outlined by Hill are:

- The Strength of the human association;
- The Consistency of the human association;
- The Specificity of the human association;
- Temporality (do biologically realistic temporal relationships exist);
- Biological gradient (i.e., the principle of dose-response where within some range of doses the incidence of the response increases with increasing dose);
- Biological plausibility (the response in humans is likely to be consistent with the observed response in animal tests, or would be predicted from the known animal toxicity and mechanism of action for that toxicity);
- Coherence (there is an internal and external consistency with all of the evidence);
- Experiment (the response decreases or increases with corresponding decreases or increases in exposure); and
- Analogy (structure activity relationships with other chemicals suggest the chemical should be capable of producing the toxicity of interest).

81. It is well recognized within the scientific/medical community that the above criteria form the scientifically-accepted basis for establishing general causation. These or very similar criteria have been adopted by the World Health Organization (WHO, 1987), the International Agency for Research on Cancer (IARC, 2006), the USEPA (USEPA, 2005), and the American Conference of Governmental Industrial Hygienists (ACGIH, 2015). The fundamental issues of general causation are generally addressed in the scientific literature. However, specific causation (i.e., whether the exposure incident in question caused a

particular individual or population's specific health effects) cannot be answered by the scientific literature alone. The fact that a chemical may be capable of producing various health effects does not mean that a particular person's or population's specific adverse health effect is a direct result of the exposure incident.

82. The process for establishing specific causation has also been established in the scientific literature for many years (Sackett et al., 1991; Sullivan and Krieger, 1992; Guzelian et al., 2005). Assuming that general causation has been established for a given chemical(s) and disease(s) or adverse health effect(s), the following additional steps must be fulfilled to establish specific causation:

1. The exposure was of sufficient magnitude (concentration and duration) to produce the alleged health effect (satisfying the principle of dose-response).

2. The chemical exposure was temporally related to the onset of the alleged health effect (satisfying the principle of temporality).

3. Potential alternate causes of the health effect (confounders) can be adequately ruled out (eliminating alternative possible etiologies for the condition).

4. There is coherence and consistency in the evidence evaluated in the specific case (establishing that the evidence is consistent with all scientific facts and beliefs).

GENERAL CAUSATION EVALUATION

83. I have reviewed the available scientific literature regarding consumption of DMAA. This review has been conducted to determine what adverse health outcomes may result from consumption of DMAA in dietary

supplements at recommended doses and directions. The weight of evidence from data found in the peer-reviewed, published scientific literature and the DoD DMAA safety panel assessment does not indicate that consumption of DMAA at labeled doses in dietary supplements, including those manufactured by Hi-Tech, will likely result in adverse cardiac or thermoregulatory injuries.

CASE REPORTS

84. To date, the available data regarding the purported association of ingestion of DMAA as a dietary supplement and adverse health outcomes are in the form of published case reports. I have reviewed, summarized, and evaluated the following case reports using the methods of specific causation to assess the strength of association of DMAA consumption and adverse health effects.

85. Archer et al. (2015), reported the death of a 30-year old female who collapsed while running the last mile of a marathon. This case report discussed the clinical manifestations of cardiorespiratory arrest, but little effort to evaluate probable causes was described. The study authors' analysis of post-mortem whole blood samples demonstrated that, in addition to DMAA, caffeine, ethanol, diazepam, and pseudoephedrine were detected. Without ruling out any of these other substances as potential contributors, the alleged cause of death was attributed to extreme physical exertion with concomitant ingestion of DMAA. Despite well-known cardiovascular effects of the other substances and their combinations (i.e.

hypotension and reflex tachycardia from diazepam, vasoconstriction effect from pseudoephedrine, etc.), Archer et al. did not consider the possible role of those substances as putative agents or contributors to death. No family history or other potential confounders were considered. Other than the temporality of DMAA consumption being met, it is unclear why the authors allege that DMAA was the cause of the death.

86. Armstrong et al. (2012), reported the case of an active duty 32-year old Navy sailor who presented to the emergency room with chest pain and shortness of breath at least 7 hours after reportedly consuming a supplement containing DMAA at the recommended dose prior to his workout. Upon admission, an electrocardiogram revealed atrial fibrillation and increased heart rate with no ST segment changes. Further examination produced a complete metabolic panel that appeared normal with the exception of elevated creatine kinase. The presence of elevated kinase with normal troponin and myocardial creatine kinase levels is suggestive of skeletal muscle injury, but not cardiac injury. Evaluation of his family history was notable for maternal heart defects. After symptomatic treatment, the patient was discharged and had an uneventful recovery. The cardiac symptoms and clinical endpoints reported by the study authors are inconsistent with the lack of the same findings in a clinical study of 50 individuals (Bloomer et al., 2013)

87. Two case reports of active duty military fatalities were reported by Eliason et al. (2012). The first case was a 22 year-old male soldier who experienced leg cramps and collapsed while running with his battalion. After four hours of resuscitative efforts, the soldier was declared dead. Hyperthermia along with renal insufficiency and elevated blood levels of cardiac and muscle enzymes contributed to the determination that shock and heat stroke were the cause of death. Analysis of a postmortem blood sample indicated the presence of DMAA. The second case was a mildly obese 32 year-old female who collapsed while nearing completion of a 2-mile physical fitness test. Upon examination, she showed no signs of pulse and was hyperthermic (significantly high core body temperature). Metabolic analysis showed parameters indicative of metabolic acidosis and liver dysfunction without reports of abnormal creatine kinase or cardiac injury. Eliason et al (2012) indicate that the quantities of various supplements she was taking, and the time period over which she was taking them, were unknown.

88. Foley et al. (2014), reported a series of cases where active duty service members known to be consuming OxyElite Pro ™, as well as several other supplements, presented to emergency rooms with signs of liver failure, including elevated blood levels of bilirubin and liver enzymes. There was significant variation in frequency and duration of dietary supplement use reported by the cases. While several cases described regular consumption of DMAA-containing

supplements for 2-3 years, others reported taking the supplements for less than a week. However, there were no data reported for blood levels of DMAA. None of the cases reported cardiovascular symptoms such as those reported by case report authors to be linked with DMAA consumption (Eliason et al., 2012; Armstrong et al., 2012). The temporality criterion for DMAA-related liver injuries would be met for these cases, and exclusion of certain liver-causing conditions was considered. However, the study authors provided no other support for their conclusion that DMAA ingestion was the most likely cause of these injuries.

89. Gee et al. (2010, 2012), reported four cases of cerebral stroke that occurred temporally with recreational use of DMAA as a party drug at doses up to ten times higher than would be recommended in dietary supplements. Cases were described for 21- and 41-year-old males who sustained basal ganglia hemorrhages. The study authors also reported a 23-year-old female who sustained a right frontal subarachnoid hemorrhage and a 36-year-old male who sustained a right intraparenchymal hemorrhage. All of these injuries reportedly occurred after ingestion of "party pills" that contained up to 600 mg of DMAA. Concomitant alcohol consumption was reported in 3 of the 4 cases, and the 4th case reported that DMAA ingestion took place while at a bar. It is well known that moderate to high alcohol consumption is a risk factor for both intracerebral and subarachnoid hemorrhage (Camargo Jr., 1989) as well as stroke (Gill, 1986). Upon admission

into the emergency room, two of the four subjects were hypertensive, while the other two were not, an important inconsistency in hemodynamic symptoms. Toxicological analyses indicated DMAA blood levels ranging from 760 to 2310 µg/L, up to 100 times higher than those observed in blood of the active duty military reported above (Eliason et al., 2012) and in clinical trial subjects ingesting 25 mg of DMAA alone (Schilling et al., 2013).

90. Another case report associating the use of a DMAA-containing dietary supplement with a midbrain thalamic hemorrhage (stroke) was reported by Young et al., (2012). These study authors described a 26-year-old active duty soldier who had reportedly been taking the supplement for about 3 weeks prior to the event. The soldier reported consuming 3 scoops of the supplement powder as a single dose, which is the maximum amount recommended by the manufacturer to not be exceeded during a 24 hour period, and triple the serving size recommended on the label. Soon after consuming the supplement and following his usual workout routine, the soldier noted a headache that continued throughout the day. He was admitted to the hospital that night, where a CT scan revealed a midbrain thalamic hemorrhage. Medical history was significant for tobacco use (a pack/day for four years) and use of a "hormone supplement" with associated unspecified behavioral issues. Given these potential confounders, the study authors concluded that it was unclear whether the hemorrhagic stroke was a result of dietary

supplement use or other predisposing factors, and suggested that consumption of the DMAA-containing supplement could have been merely coincidental and not causal (Young et al, 2012).

91. Karnatovskaia et al. (2015), reported a case of a 21 year-old who suffered a cardiac arrest while exercising at a gym. Upon arrival to the emergency room, electrocardiogram showed diffuse ST-segment elevation without QT prolongation, indicative of possible myocardial infarction (Wang et al., 2003), but inconsistent with the normal electrocardiograms observed in other DMAA-related case reports (Armstrong et al., 2012). Similarly inconsistent with other DMAA-related case reports and clinical trial data (Bloomer et al., 2013), this patient showed elevation of cardiac enzymes indicative of injury (elevated myocardial creatine kinase). This finding was likely secondary to myocardial infarction. After recovery, the individual reported that on the day of admission into the emergency room, he had consumed a dietary supplement for the first time before exercising. Analysis for the presence of amphetamine, ephedrine and other drugs was conducted, but no data for presence of DMAA was mentioned. The absence of supporting clinical data, but attribution of effects to DMAA exemplifies how assumptions of DMAA toxicity may result in causal associations based only on a temporal coincidence between an adverse health outcome and consumption of a dietary supplement.

92. Salinger et al. (2011), reported a case of a 24 year-old that presented to the emergency room with symptoms of headache, heart palpitations, nausea/vomiting, and chest pain one hour after ingesting a DMAA-containing dietary supplement, which contained caffeine, DMAA, and other ingredients. He presented with blood pressure of 180/100 mmHg and a heart rate of 130 bpm. His echocardiogram also was indicative of a cardiomyopathy. The patient reportedly used higher product doses than recommended on the label in order to achieve a more pronounced, "energized" state. This case report simply concluded that a temporal association existed between the consumption of the dietary supplement and the symptoms, without making any suggestions for a causal relationship. In fact, the study authors concluded that, "*Additional data is needed to implicate DMAA alone or in combination with caffeine as a pharmacological trigger [of cardiopulmonary injury]*."

93. Smith et al. (2014), reported a case of a 22-year-old male who presented with angina chest pain, and was diagnosed by the study authors to have suffered an acute myocardial infarction (i.e., heart attack) the previous day while coaching basketball. The subject had been consuming for three weeks two dietary supplements containing either DMAA or synephrine alkaloid extract of the plant *Citrus aurantium*, both of which possess sympathomimetic activity. The study authors did not report the amounts ingested of either dietary supplement. Further

medical evaluation of the subject revealed a thrombotic embolism (blockage) of the descending coronary artery. The study authors concluded that the coronary artery blockage was caused by use of one or both of the dietary supplements. However, they did not offer any evidence or cite previous medical or scientific research as a basis for the existence of such a disease mechanism.

Specific Causation Evaluation

94. Even though general causation has not been satisfied for the published case reports, I considered whether the case reports contained sufficient data to establish *specific* causation implied by the FDA, based on a few case reports. The following points serve as the basis for my opinion that general and specific causation have not been established for adverse health effects and injuries caused by DMAA consumption at levels recommended by Hi-Tech product labeling.

1. Qualitative Toxicity - the chemical in question is known to be capable of producing the alleged effect in humans. [This is essentially the result of the general causation analysis.]

The available human clinical data for DMAA ingestion does not indicate that DMAA is capable of causing adverse effects related to cardiac, liver, kidney, or thermoregulatory health. The published case reports for vascular effects are insufficient to establish specific causality due to confounding factors such as

concurrent use of multiple dietary supplement stimulants other than DMAA and caffeine, as well as ethanol consumption.

2. Dose-Response - the individual was exposed to the chemical and the amount of chemical was absorbed into the body at sufficient magnitude and duration to be capable of producing the alleged effect.

While case report authors reporting the use of DMAA as a recreational drug at high (and possibly underreported) amounts and concurrent adverse health outcomes (Gee 2010, 2012), evidence of adverse health effects resulting from consumption of DMAA at levels such as those recommended on Hi-Tech's labels (i.e. 45-90 mg) was not observed in controlled clinical trials (Bloomer 2011a, 2011b; McCarthy 2012a, 2012b; Farney et al., 2012; Whitehead et al., 2012; Bloomer et al., 2013). The human clinical trial data show that blood concentrations resulting from consumption of DMAA at concentrations approximating labeled serving sizes in dietary supplements would be significantly lower than those observed in case reports of recreational use and injuries to military active duty personnel. These discrepancies between DMAA abuse and labelled use as a dietary supplement product emphasize the importance of evaluating DMAA safety in the context of a dose-response relationship and not solely from extreme exposures. There is no evidence to indicate that consumption of DMAA at doses

recommended in Hi-Tech's products would be sufficient to elicit adverse health effects described in the published case reports or implied by FDA.

3. Confounders - all other significant causes (including exposure to other substances, lifestyle, workplace, and inheritable factors) of the disease for the individual have been controlled for or ruled out.

The published case reports described above are anecdotal observations that generally lack dose measurements or estimates, evaluation of pre-existing conditions, or confounding co-exposures to other compounds that are known to result in the reported health effect. Recognizing that differences exist between differential diagnosis and causality assessment (using specific methodological approaches for general and specific causation), the published case reports have multiple confounders that, if not ruled out, limit the use of the reports to establish or support a claim of causation.

5. Coherence - all of the evidence is consistent with the conclusion of specific causation.

Overall, there is insufficient coherence and consistency between the case reports and the published human clinical trials to establish a causal relationship between FDA's implied adverse outcomes and consumption of DMAA at concentrations found in Hi-Tech's supplements. The paucity of AERs for Hi-Tech products relative to total sales of DMAA-containing supplements from Hi-Tech

between 2005 and 2015 (discussed below) is indicative of DMAA's safety as a dietary supplement.

95. A lack of coherence is apparent in case reports that differ markedly in clinical profiles, symptoms and diagnoses of users of DMAA-containing supplements. For example, Armstrong et al. (2012), showed that the alleged consumption of DMAA effected no changes in cardiac markers of injury, metabolic panel, or abnormalities in ST-segment of the electrocardiogram conducted on the patient. However, Karnatovskaia reported symptoms consistent with cardiac injury and myocardial infarction (Karnatovskaia et al, 2015). Similarly multiple case reports showed cardiovascular effects with no abnormalities in liver function (Gee et al, 2010, 2012; Salinger et al., 2011; Young et al., 2012), whereas others showed signs of liver failure without cardiovascular symptoms (Foley et al., 2014).

96. My evaluation of the scientific literature does not indicate that oral consumption of DMAA at recommended labelled doses of Hi-Tech's products is causally linked to adverse health effects described in the published case reports or implied by FDA. FDA's statements that DMAA is unsafe and increases the risk of cardiovascular events are inadequately substantiated and are not supported by the scientific literature, nor do they satisfy the criteria of strength of association, specificity, dose-response, consistency, or coherence for the development of

DMAA-induced adverse health effects. Therefore, it cannot be concluded to a reasonable degree of scientific certainty that adverse health effects implied by FDA are attributable to the consumption of DMAA at recommended dose levels of Hi-Tech products.

FDA ADVERSE EVENTS REPORTING DATA COMPARISON

97. The FDA maintains a database of adverse events reports submitted by pharmaceutical and dietary supplement makers and individuals (FDA, 2015). The database is part of the FDA Adverse Event Reporting System (CAERSCAERS). In its webpage regarding DMAA safety (FDA, 2013), FDA stated that it had received 86 adverse event reports of psychiatric disorders, heart problems, nervous system disorders, and death that occurred with consumption of unknown quantities of dietary supplements, possibly including DMAA-containing products. Forrester (2013), reported that 39 of 56 (83%) 2010-2011 DMAA-related calls to the Texas Poison Center Network were categorized as non-serious in nature. The quality of the data for each adverse event report is dependent solely on the company or individual submitting the report. The addition of an adverse event report to the database does not require the inclusion of accurate data for dose, ingestion frequency, or confounding factors such as concurrent medication or dietary supplement use or health status. As such, the CAERS data should be used to flag

products for more in-depth investigation, but not to definitively associate health effects with product use.

98. I reviewed the results provided to me by Counsel of a Freedom of Information Act (FOIA) request for data extracted from the CAERS database regarding adverse event and ingestion of DMAA and/or Hi-Tech products from July 22, 2005 to April 29, 2015 (FDA, 2015). During this 10-year period, there were 35 reports involving Hi-Tech products, of which six reports listed DMAA specifically as an ingredient in the product consumed, and 29 reports did not include DMAA as an ingredient or listed ingredients as "unknown." Of the six reports that listed DMAA-containing Hi-Tech products, three reported physician or emergency room visits, and three reported non-serious adverse events. According to Hi-Tech sales data provided to me by Counsel, there were 3,755,578 units of DMAA-containing dietary supplements sold by Hi-Tech from October of 2010 through 2015. Each of the units sold contained 25-100 ingestible dietary supplement capsules. If one assumes that only one capsule was consumed per unit sold (a hypothetical lower bound estimate), then 3,755,578 capsules of Hi-Tech's DMAA-containing product would have been consumed in the last 5+ years. Alternatively, if every capsule from every purchased unit was consumed, then 205,674,645 total Hi-Tech DMAA-containing product capsules would have been consumed in the last 5+ years. I did not have sales data for 2005 through

September 2010. Nevertheless, the 35 reported AERs resulting from ingestion of over 3.7 million to 205 million servings of DMAA-containing dietary supplements is not remotely indicative of the presence of a hazardous dietary supplement product in the marketplace.

99. To put these CAERS reports into perspective, I downloaded all of the CAERS database files from 4th quarter of 2012 through 2014 and searched for AERs associated with consumption of multivitamin or vitamin C products (CTEH, 2015). For vitamin C products, there were 4,771 AERs, of which 7 were associated with death and 2,530 were categorized as life threatening, disabling, or requiring hospitalization. For multivitamins, there were 24,128 AERs, of which 3,143 were associated with death, and 13,792 were categorized as life threatening, disabling, or requiring hospitalization. These AERs were from a total pool of 1,022,969 AERs for which outcomes were recorded. Thus, from 2012 to 2014, there were 55-times and 281-times more CAERS adverse event reports with serious outcomes for vitamin C and multivitamins, respectively, than for Hi-Tech DMAA-containing products reported from late 2010 to 2015. This comparison does not suggests that vitamin C or multivitamin dietary supplements incur a higher risk of adverse health effects than DMAA; there are likely far more vitamin C and multivitamin product users in the U.S. than DMAA-containing product users over this time period. It does, however, suggest that the CAERS data should be

used as a trigger for further, more rigorous investigation, but not for establishing disease causation or for serving as the sole basis for public health declarations.

CONCLUSIONS

100. I have been asked to evaluate the safety of DMAA at levels that would be found in dietary supplements such as those manufactured by Hi-Tech based on the available scientific literature and evidence. My analysis included a review and analysis of animal toxicity studies, clinical trials, an epidemiology study, and case reports allegedly associating adverse health effects with the consumption of DMAA in dietary supplements. Although exposure to DMAA can lead to modest increases in systolic and diastolic blood pressure, tremors and other symptoms at sufficient concentrations and dose exposures (i.e. >100 mg doses), there is no evidence that consumption of DMAA at concentrations found in Hi-Tech's dietary supplements and according to labeled doses would result in any adverse health effects.

101. A scientifically-defensible causal association between consumption of DMAA at levels found in Hi-Tech's dietary supplements and adverse health outcomes cannot be supported with the available scientific data in humans and animals.

DISCLOSURE

102. I was engaged by Epstein, Becker, & Green to provide expert opinions regarding the safety of DMAA for use as an ingredient in dietary supplement products produced by Hi-Tech Pharmaceuticals, Inc. My employer, CTEH®, was compensated at the rate of $335/hour for my services provided. The opinions proffered in this Declaration are my own. None of the opinions in this document were drafted by individuals from Epstein Becker, & Green or Hi-Tech Pharmaceuticals, Inc. My opinions are given to a reasonable degree of scientific certainty.

103. I reserve the right to update this report should additional relevant information become available.

Respectfully Submitted

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APPENDIX A

CURRICULUM VITAE OF MICHAEL H LUMPKIN, PHD, DABT

EXPERIENCE

Dr. Michael Lumpkin is a board-certified toxicologist with more than 14 years of experience in dose reconstruction, chemical dose response assessment, physiologically-based pharmacokinetic (PBPK) modeling, chemical emergency response, product stewardship and safety assessments, and litigation support. Michael has developed, critiqued and applied PBPK models for volatile organic compounds (VOCs), metals, pesticides and bioterrorism agents for USEPA, CDC and DOD, for use in regulatory standard support and emergency planning. He has developed a framework and performed safety assessments of dietary supplement products. He has coauthored numerous peer-reviewed hazard assessments for USEPA and the Agency for Toxic Substances and Disease Registry (ATSDR). He has provided critical reviews and analyses of toxicology data for numerous compounds, including formaldehyde, PAHs, inhaled dust and perchlorates. Michael has provided analyses of human and animal study data in support of new drugs and medical device applications, and has designed and performed occupational exposure reconstructions for VOCs and diisocyanates using laboratory simulations. He has developed novel occupational exposure limits for pharmaceutical and industrial chemicals. Michael has served on ad hoc federal grant review committees and as a peer reviewer for toxicology journals, and has lectured in graduate courses and emergency responder seminars for inhalation toxicology and risk assessment. He is a member of the Society of Toxicology and is certified as a Diplomate of the American Board of Toxicology.

EDUCATION

Ph.D., Toxicology Athens, Georgia	2002	University of Georgia
B.S., Biochemistry Athens, Georgia	1994	University of Georgia

REGISTRATIONS & CERTIFICATIONS

Diplomate, American Board of Toxicology – 2008, 2013
40 Hour HAZWOPER
8 Hour HAZWOPER Supervisor
TWIC Clearance
Firefighter I (NFPA 1001), National Board on Fire Service Professional Qualifications (2001)

PROFESSIONAL AFFILIATIONS

Member, Society of Toxicology (2003-Present)
Councilor, Risk Assessment Specialty Section of the Society of Toxicology (2014-2016)
President, Southeastern Regional Chapter of the Society of Toxicology (2011-2013)

EMPLOYMENT PRIOR TO JOINING CTEH®

2010 – 2014 Senior Toxicologist / ENVIRON International Corporation, Arlington VA
2004 – 2010 Senior Toxicologist / Syracuse Research Corporation (now SRC, Inc.), N. Syracuse, NY
2002 – 2004 Toxicologist / Clayton Group Services (now Bureau Veritas), Kennesaw, GA
1994 – 1998 Research Coordinator / TRS Labs, Inc., Athens, GA

EXPERIENCE

Incident Response

- Served as the lead toxicologist of a team responding to a major crude oil unit train derailment and fire, including interaction with U.S. Coast Guard, Federal and State regulators, local fire and law enforcement leadership, and community members.
- Served as the lead toxicologist of a team responding to a gasoline pipeline release and a petroleum refinery tank failure, including interaction with client environmental health professionals and members of the unified command.
- Provided toxicological support for a multidisciplinary team addressing chemical vapor exposures to workers at the U.S. Department of Energy Hanford nuclear site.
- Conducted air monitoring for multiple HazMat train derailments, petroleum pipeline releases, and industrial and natural gas well fires across the U.S.
- Provided toxicological and public health information to residents following a crude oil pipeline spill into the Yellowstone River in Montana.
- Provided toxicological support to railroad HazMat managers and emergency room attending physicians following worker chemical exposures resulting from a train derailment.
- Responded to and reported on health risk outcomes from a small-scale industrial chemical spill at a major aircraft manufacturing facility. The final risk assessment and communication report successfully allayed concerns within the exposed workforce for future health risks.
- Assessed likely health impacts of perchlorate exposures following an accidental release into a municipal drinking water system.
- Advised dietary supplement client on technical responses to alleged injury

outbreak, including management of technical meetings with FDA and CDC investigators, and technical briefing of U.S. congressional staff.

PBPK Modeling and Pharmacokinetic Analysis

- Developed a rodent and human model for inhalation of benzo[a]pyrene for use in regulatory dosimetry and risk assessment.
- Developed rodent models for drinking water disinfection byproducts during pregnancy, and halogenated hydrocarbons for use in human health risk assessment.
- Developed prototype inhalation models for bioterrorism agents (anthrax and tularemia) in nonhuman primates capable of predicting internal doses deposited in the lungs and distributed through the lymphatic and circulatory systems.
- Developed preliminary PBPK models for inhaled polycyclic aromatic hydrocarbons (PAHs).
- Reviewed, critiqued and applied PBPK models for a variety of organic compounds including:
- Applied PBPK and benchmark dose models for acrylonitrile, dichloromethane and 1,4-dioxane in support of cancer and non-cancer dose-response chapters of USEPA IRIS toxicological reviews.
- Provided review and critique of PBPK models in support of USEPA IRIS assessments (vinyl acetate, carbon tetrachloride, tert-amyl methyl ether and n-butanol) and ATSDR toxicological profiles (benzene, ethylene glycol, vinyl chloride, phenol, perchlorate and diazinon).
- Provided analysis and interpretation of human pharmacokinetic data, including implications for drug safety, to pharmaceutical and dietary supplement manufacturers.
- Provided critical review and comparison of human pharmacokinetic data sets for combination oral contraceptive products.

Chemical Product Stewardship

- Provided toxicological support to a polystyrene manufacturer's investigation of customer-reported occupational dermatitis incidents.
- Developed a novel occupational exposure limit for a reaction product formed during manufacture of flexible medical tubing.
- Developed novel occupational exposure limits for cancer chemotherapy and testosterone-based drug products.
- Developed a novel occupational exposure limit for a manufacturing by-product compound using "read across" methodology.
- Developed multiple OSHA/GHS-complaint Safety Data Sheets (SDSs) for petrochemical and food products.
- Performed California Proposition 65 Safe Harbor analyses for a variety of consumer products.

Chemical Toxicity Value Derivation

- Provided updated dose-response assessments to clients based on newly available data for metals, VOCs and aldehydes.
- Developed evidence-based assessment of perchlorate drinking water standard and research priorities, presenting finding to an EPA SAB, at national scientific meetings, and to a major trade association.
- Provided critical comments pertaining to interpretation of toxicokinetic, mode of action and dose-response data for carcinogen toxicity assessments such as formaldehyde and PAHs.
- Co-authored toxicokinetics and dose-response chapters, including dose-response modeling of toxicity data to derive reference doses and concentrations, and cancer potency factors, for numerous USEPA IRIS toxicological reviews and peer-reviewed provisional toxicity value documents for solvents, metals and aldehydes.
- Authored toxicity chapters and derived non-cancer minimal risk levels for numerous ATSDR toxicological profiles for VOCs, metals and pesticides.

Dose Reconstruction

- Derived dose estimates of asbestos fiber exposure for a variety of industrial settings.
- Designed and managed a laboratory dose reconstruction assessment of inhalation and dermal exposure to diisocyanates and other VOCs under simulated occupational conditions.
- Analyzed air sampling and exposure factor data to determine allowable PCB exposures in public school students.

Pharmaceutical Product Development

- Provided interpretation of human pharmacokinetic data in support of an FDA new drug application.
- Authored safety assessments of surgical implant devices in support of FDA approval for conduct of human trials.

Dietary Supplement Safety Assessment

- Developed a framework for client to use in study design and data interpretation for developing product-specific safety assessments.
- Performed safety assessments for multiple dietary supplement products
- Helped client interpret pharmacokinetic data and design human clinical trials for assessing safety of high-cocao flavanol content supplements.
- Designed and monitored preclinical rodent toxicity studies for dietary supplement product ingredients.

Litigation Support

- Provided expert deposition testimony for a cases involving occupational ammonia, chlorine gas, and methylene chloride gas exposures, ethanol/drug pharmacokinetics and risk-based environmental health litigation.
- Provided risk-based analysis, expert reports, and expert deposition testimony regarding health impacts related to offsite groundwater VOC migration from a municipal landfill and residential pesticide exposures.
- Contributed to health impact assessment and expert report development in cases involving public exposures to bisphenol A, coal ash wastes, contraceptive hormones, landfill odors, as well as occupational exposures to Naturally Occurring Radioactive Materials (NORM), asbestos, 1,3-butadiene, diisocyanates, mixed VOCs and World Trade Ce nter dust.
- Analyzed the effect of pharmaceutical incipients on gastrointestinal absorption and cellular effects of an osteoporosis medication.
- Developed exposure modeling methods to compare disease risks over time in students and workers exposed to PCBs from aging lighting systems in a major metropolitan public school system.
- Developed exposure scenarios and risk-based exposure limits for PCBs in air of public school buildings.
- Assisted with future projections of population-level blood PCB levels in based on NHANES data.

PUBLICATIONS

A. Peer-Reviewed Publications

1. Campbell, J, Franzen A, Van Landingham C, Lumpkin M, Crowell S, Meredith C, Loccisano A, Gentry R, Clewell C. 2016. Predicting lung dosimetry of inhaled particleborne benzo[a]pyrene using physiologically based pharmacokinetic modeling. Inhal Toxicol.28: 520-535.

2. Rodricks J and Lumpkin M. 2013. DMAA as a Dietary Ingredient. JAMA Intern Med. 173:594-595.

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