

EXHIBIT 4

UNITED STATES DISTRICT COURT

EASTERN DISTRICT OF LOUISIANA revisions to p. 33- new material is highlighted

KATHLEEN MOLLER,

Plaintiff,

v.

**MARTIAN SALES, INC.; JOPEN,
LLC; JOHNSON FOODS, LLC; LP
IND., LLC; CAG HOLDINGS, LLC;
RMH HOLDINGS, LLC; ABC
INSURANCE COMPANY and John
Does 1-4,**

Defendants.

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CIVIL ACTION NO.

2:24-CV-228-WBV-DPC

THE HONORABLE WENDY B. VITTER

**MAGISTRATE JUDGE DONNA PHILLIPS
CURRAULT**

EXPERT REPORT OF JACK E. HENNINGFIELD, PH.D.

1. I have been asked by Defendants to review relevant medical records and other documents and render a professional opinion regarding the current state of the science concerning kratom's chemistry, pharmacological effects, safety, reasons for use, why kratom is considered to be an important public health asset by leading kratom science experts, and federal agencies that have the authority to ban kratom.

2. I have developed this report to address scientific, regulatory, and public health issues within my expertise as it pertains to kratom safety, reasons for use, effects, and potential for abuse and physical dependence (commonly referred to as "addiction potential"). My opinions are my own and do not necessarily reflect those of any of the many organizations I have been affiliated with in the past or present.

3. My work is through my employer, Pinney Associates, which is compensated at a rate of \$800 per hour for work performed through December 31, 2024, and at a rate of \$850 per hour for work performed through December 31, 2025. Pinney Associates compensates me at a rate of \$148.75 per hour in addition to my base salary for my work on this matter. My compensation is neither contingent on the outcome of this matter nor the conclusions reached in this report.

4. My opinions are based on my five decades of training and research, regulatory experience, advising companies in support of their efforts with the United States Food and Drug Administration ("FDA"), as well as contributing to the development and submission of New Dietary Ingredient Notifications ("NDIN") to the FDA for kratom products. My opinions also reflect my published research and expert reports, commentaries, and review articles that have addressed kratom and evolved along with the rapidly emerging science over the past decade. My opinions are to a reasonable degree of scientific and regulatory certainty. Together, my own

research, collaborations with other researchers, and professional regulatory experience provide the foundation for my summary of the current state of kratom science and rebuttal of key opinions within my area of expertise offered by Plaintiff's experts and alleged in the Third Amended Complaint.

5. A copy of my current *curriculum vitae* (including testimonial history) is attached as Appendix A.

6. A list of the documents referenced and reviewed is attached as Appendix B.

BACKGROUND AND QUALIFICATIONS

7. My relevant experience began with my work in a leading neuropharmacology and abuse potential testing laboratory in 1971 while an undergraduate student. In 1974, I graduated from the University of Minnesota with a major in psychology with honors, summa cum laude. I was invited to apply to and was accepted as a U.S. Public Health Service Fellow at what was then the lead psychopharmacology training program in the U.S. This program, based at the University of Minnesota, was established to train generations of researchers in addiction science, neuropsychopharmacology, evaluation of potentially addictive substances, addiction treatment, and addiction control-related public policy. My training included pharmacology and its specialty branch, toxicology. I received my PhD in Experimental Psychology with a supporting program in pharmacology from that program in 1977. I was then awarded a National Council on Alcoholism research fellowship to continue my research.

8. In 1978, I was recruited to a faculty position at the Johns Hopkins University School of Medicine, where I am presently Adjunct Professor of Behavioral Biology, Part Time, in the Department of Psychiatry and Behavioral Sciences. I was recruited to the National Institute on Drug Abuse (NIDA) Intramural Research Program ("Addiction Research Center") housed on the Johns Hopkins Baltimore, Bayview campus in 1980 where I remained until 1996.

9. My appointments at NIDA included service as Chief of the Biology of Dependence and Abuse Potential Section and Chief of the Clinical Pharmacology Branch. My responsibilities included conducting research to evaluate the safety and addictiveness of known and potentially addictive substances, as well as potential addiction treatment medicines. Beginning with my research and regulatory responsibilities at NIDA until the present, I have contributed to the development and/or regulatory approval of most of the medicines presently approved by the FDA for treating opioid, tobacco and alcohol use disorders and withdrawal ("addictions").

10. My work at NIDA included contributing to the regulation of potentially addictive drugs and substances, such as prescription medicines and tobacco products. This included work with the FDA and the DEA on matters pertaining to addiction science, abuse potential assessment, and Controlled Substances Act drug scheduling. My NIDA position involved advising several Surgeons General, including Dr. C. Everett Koop, and several FDA commissioners, including Dr. David Kessler (from whom I received service awards for my addiction research and contributions to substance control and regulation).

11. Most of my FDA regulatory work while I was a NIDA employee was focused on abuse potential assessment of various substances (e.g., cannabinoids, heroin, smoked cocaine, and

tobacco products), and pharmaceutical products in development including the partial opioid agonist buprenorphine and a broad range of others. In the 1990s, my work was extensively focused on potential regulation of cigarettes and smokeless tobacco products working directly with FDA Commissioner David Kessler and senior scientific and legal staff from FDA, including those representing three FDA centers collaborating on the development of an appropriate regulatory approach to tobacco products, which raised many novel issues. This included the FDA's Center for Devices and Radiological Health ("CDRH"), Center for Drug Evaluation and Research ("CDER"), and Center for Food Safety and Applied Nutrition ("CFSAN").

12. From 1994 until I left NIDA on September 1, 1996, I was officially on a part time "detail" to serve FDA in this regulatory development by order of the Secretary of Health, while maintaining my NIDA responsibilities as Chief of the Clinical Pharmacology Branch and the Biology of Dependence and Abuse Potential Assessment Section. During my tenure, the Dietary Supplement Health and Education Act of 1994 ("DSHEA") came into effect, and FDA's thinking about how to regulate dietary supplements was evolving in parallel to its thinking on regulating tobacco products. An important focus of the FDA during this time was food and dietary supplement standards for evaluating safety, purity, and labeling in the context of public health, as well as practical considerations for product development and manufacture. I was among the FDA team members on this regulatory effort invited to DHHS and White House Ceremonies in 1996 and at the passage of the Family Smoking and Tobacco Control Act in 2009. I also received an award from the Secretary of Health and Commissioner of the FDA for my service in regulatory development.

13. Additionally, I represented NIDA in various congressional hearings and FDA briefings. I was detailed at times to serve on various FDA committees involved in drug and tobacco regulation and various U.S. Surgeon General's reports on addiction-related issues, including the prevention and treatment of substance abuse and addiction.

14. Since leaving NIDA, I have served on several governmental committees and as a Special Government Employee at the FDA CDER and separately for the FDA Center for Tobacco Products. I was invited by the World Health Organization ("WHO") to serve on its inaugural Scientific Advisory Committee and then its Tobacco Regulatory Study Group based on my expertise in addiction, abuse potential assessment and substance regulation. I served the WHO from 2001 to 2014.

15. While at NIDA, with outside activities approval, and since leaving NIDA, I have served as an expert witness in matters related to addiction science, treatment and prevention. This included serving as the lead addiction witness for state attorneys general against the tobacco industry in the late 1990s and for the U.S. Department of Justice against the tobacco industry in the early 2000s.

16. My work at NIDA included a focus on addiction treatment development. These efforts began with buprenorphine for opioid use disorder and pain management at NIDA in 1980, nicotine gum for tobacco use disorder and withdrawal in 1982, and naltrexone for opioid use disorder in the mid-1980s. Later, these efforts also included nicotine gum, patch, nasal spray, a nicotine vapor device, and other tobacco addiction treatments and substitutes. Through my research at NIDA and Johns Hopkins and consulting with Pinney Associates, I have been involved

in the development and regulatory approval of most of the FDA-approved treatments for opioid, tobacco, and alcohol addiction and a broad range of medicines for other disorders including those related to ADHD, epilepsy, opioid overdose prevention, various types of pain, and others. I have also given invited testimony to Congress, the FDA, and the White House on the importance of providing less harmful alternatives for people who continue to use addictive substances.

17. My research and responsibilities at NIDA included consideration of the benefit-risk balancing that public health institutions, such as the Centers for Disease Control and Prevention (“CDC”), FDA, and international bodies, take into account in their regulatory and other substance policy efforts to advance public health. As listed in my CV, I regularly publish and present state of the art reviews on these topics, often along with former FDA and DEA officials and at times FDA staff.

18. My work on kratom product research, product assessment, and regulation began in 2014 working with a former FDA Office of Dietary Supplement staff member and legal regulatory consultants on kratom product submissions to FDA, labeling and other issues. I am a leading kratom scientist. I have published nearly 500 scientific articles, monographs, and books of which most have been peer reviewed. These include 17 original research articles and reviews of kratom abuse and dependence potential, safety, toxicology and public health impact, and 5 joint scientific expert reports and comments to federal agencies and the White House. I have also given more than 600 presentations at scientific meetings, many of which were invited. More than 30 presentations have addressed kratom science, policy and regulatory needs.

19. As summarized in my CV, I have served on many international panels for governmental agencies and scientific organizations regarding addiction science, treatment, regulation and policy, including harm reduction. Most recently, I was accepted by the WHO Expert Committee on Drug Dependence to provide testimony on kratom safety, real world therapeutic use, and addictiveness during its 2021 review of kratom to determine if kratom should be put under one of the international drug control conventions. After considering the types of factors summarized above, the WHO and the United Nations Bureau on Drugs and Crime determined that putting kratom under international drug control treaties (which would have banned legal kratom) was not warranted. Rather, they recommended that kratom should remain under surveillance. In 2025, I was invited to the United Nations Commission on Narcotic Drugs meeting in Vienna to serve on a Roundtable Discussion Panel that addressed harm reduction approaches, including kratom and the public health benefits of its regulation.

20. I am currently Vice President for Research, Health Policy and Abuse Liability at Pinney Associates, and Adjunct Professor of Behavioral Biology, Part-time in the Department of Psychiatry and Behavioral Sciences at Johns Hopkins University School of Medicine, Baltimore.

SUMMARY OF GENERAL OPINIONS RELATED TO KRATOM SAFETY, USE, ADDICTIVENESS AND REGULATORY STATUS IN THE UNITED STATES

21. In this section I provide my foundational opinions and facts related to kratom science, public health context, and regulatory framework. These pertain to the broad universe of kratom products available and marketed in the United States, recognizing that products vary widely in their purity, efforts to assure that they are not adulterated, their alkaloid contents and

other factors. In contrast, the OPMS products alleged to have been consumed by Harmony Moller and to have caused her death are made to higher standards and compliant with the American Kratom Association's Good Manufacturing Practice ("GMP") Standards Program.

Opinion 1:

22. Kratom is not and should not be characterized as "an opioid," nor regulated as a dangerous or addictive controlled substance in the United States Controlled Substances Act ("CSA") or under the International Drug Control Conventions of United Nations. I agree with the determinations of the U.S. Department of Health and Human Services ("DHHS"), DEA and the United Nations Office on Drugs and Crime ("UNODC") that kratom does not warrant such designations or control.

Opinion 2:

23. Kratom is not characterized by "high abuse," "dependence" or "addiction" potential and is well within the range of many licit consumer dietary substances and health products (e.g., caffeine, antihistamines, and CBD) that are abused and can be addictive in some people but overall are used primarily for their beneficial and otherwise useful health and/or life-enhancing effects.

Opinion 3:

24. Kratom does not carry a high risk of death. To the contrary, the risk of death by kratom alone appears very low and rare. This has also been the conclusion of NIDA and DEA for approximately a decade and similarly concluded by FDA in 2024 after its approximately decade of review and own testing. My opinion continues to be consistent with Assistant Secretary Gior's 2018 review statement on this matter: "There is still debate among reputable scientists over whether kratom by itself is associated with fatal overdoses."

Opinion 4:

25. There is no consensus on the basis by which kratom might cause life threatening effects or death; in contrast to most substances that contribute to overdose deaths (e.g., respiratory depression by opioids and sedatives, cardiovascular incidents by stimulants).

Opinion 5:

26. There is no consensus on what level of kratom consumption or level in the bloodstream would constitute a lethal dose, in contrast to most substances of high abuse, addiction and mortality potential that contribute to the U.S. drug overdose epidemic. Specifically, there is no well-defined toxidrome for kratom, but rather kratom associated deaths most commonly involve other substances, including prescription and non-prescribed drugs, and various pre-existing disease conditions. Deaths occurring in the absence of use of other substances are rare, as concluded by NIDA (2022) and FDA (2024).

Opinion 6:

27. Kratom is an overall public health asset that is used by many people as a harm reduction approach to reduce or eliminate the use of opioids, sedatives, stimulants, and alcohol. Such public health benefits were considered in the determinations of the DEA, the DHHS, and the WHO Expert Committee on Drug Dependence not to schedule kratom as a controlled substance.

Opinion 7:

28. Most people use kratom for health and well-being, including as a supplement to, or replacement for, caffeinated beverages or to self-manage depression, anxiety, pain, or opioid and other drug withdrawal. Like many dietary substances that consumers use, the health and well-being benefits of kratom are not and cannot be approved for therapeutic use by the FDA.

Opinion 8:

29. Kratom is a legally marketed product in 44 states, and it is legal for people in those states to possess and consume kratom. Moreover, at the time of this writing, the legislatures of 18 states have passed laws to ensure legal access to kratom with varying approaches to ensure that products meet their standards for safe access and potential benefit to public health and adults who choose to consume kratom.

Opinion 9:

30. Kratom carries a low risk of producing a medical condition requiring treatment, such as Substance Use Disorder (“SUD,” also known as “dependency” or “addiction”) or withdrawal disorder (also referred to as “physical” or “physiological” dependence). However, mild to moderate SUD and/or withdrawal following discontinuation of kratom use is not uncommon in people who consume kratom repeatedly every day for at least several months. In contrast with opioid, alcohol, and stimulant use and withdrawal disorders for which treatment is often sought, most kratom users who reported dependence or addiction did not seek treatment and found it self-manageable and not debilitating.

Opinion 10:

31. The vast majority of the evidence upon which I base my opinions was generated by independent researchers primarily supported by the National Institutes of Health (“NIH”) and NIDA and not commercial kratom product developers or kratom advocacy organizations such as the American Kratom Association. Such studies have been published at an increasing rate over the past decade at leading biomedical research institutions, including Johns Hopkins, the University of Florida, the NIDA intramural program itself and many others. Only a few percent of such publications were supported by commercial companies or foundations.

Opinion 11:

32. The FDA fueled misunderstandings related to kratom safety, legal status, and benefits by its approach from 2014 to 2018 that was intended to prohibit legal kratom access and criminalize kratom marketers and consumers. More recently, the FDA ceased making statements that imply kratom has narcotic-like risks of addiction and death. However, the FDA’s website at the time of this writing is confusing in its description about kratom’s safety and regulatory status.

Opinion 12:

33. The FDA has not attempted to generally ban marketing kratom or to suggest that marketing kratom is illegal or irresponsible through its warning letters to some companies that sell kratom. In fact, the FDA states that its approach in these warning letters is to protect public health and to guide acceptable marketing practices.

Opinion 13:

34. For several years, the FDA diverged from the DEA with respect to communications related to kratom science, safety and appropriate public health policy. In the past few years, however, the FDA appears to have adopted positions that are more consistent with scientific evidence and in support of public health.

OPINIONS SPECIFIC TO PLAINTIFFS' CLAIMS

35. In this section I provide opinions specific to Plaintiff's allegations.

36. Plaintiff has not provided valid and reliable support for the allegation that kratom was the cause, or a substantial contributing factor, to Harmony Moller's death on February 6, 2023.

37. The coroner's report, as cited in the Complaint (para 33), suggests potential pre-existing heart abnormalities, e.g., "Abnormally high left coronary ostia takeoff." The coroner's report does not provide a basis for concluding that mitragynine contributed to Ms. Moller's death. I note that blood levels of mitragynine were far lower than those that are sometimes associated with death (150 ng/mL by NMS Labs and 158 ng/mL by UC). NMS labs did not find a positive result for the mitragynine metabolite, 7-hydroxymitragynine ("7-OH"), which is consistent with low kratom/mitragynine intake. However, the NMS Labs reports did identify several other pharmacological substances and metabolites.

38. Although I do not have an opinion on the actual cause of Ms. Moller's death, my scientific training and experience make clear that singling out kratom use as the primary or substantial contributor to death is confounded by Ms. Moller's potential preexisting conditions and other substance use.

39. The autopsy finding that Ms. Moller's pre-existing heart condition was "exacerbated by Mitragynine use" is speculative. There is no established scientific or medical consensus that mitragynine "exacerbates" Ms. Moller's specific and rare cardiac anomaly or causes death in such circumstances. This is distinct from substances with well-defined mechanisms of lethal toxicity (e.g., respiratory depression from classic opioids or hypertensive crisis from classic stimulants). As Eckhardt and Nickel (2023) have concluded, "Some case reports of kratom associated arrhythmia, including fatalities, have surfaced, but little is known of the mechanism of kratom-induced ventricular arrhythmia nor the depth of the problem."

40. Attributing causation to mitragynine is confounded by (a) Ms. Moller's pre-existing cardiac condition noted in the coroner's report, (b) the multiple empty liquor and prescription pill bottles (including Acyclovir, methylphenidate, hydrocodone/acetaminophen, and gabapentin) and drug paraphernalia found at the scene (*see* St. Tammany Parish Sheriff's Office Incident Report),

and (c) the toxicology report confirming the presence of multiple other drugs and substances such as diphenhydramine, promethazine, and marijuana (THC finding). Note that evidence of marijuana use is of concern because my own marijuana research and many others have found that marijuana can produce rapid and pronounced tachycardia (Heishman et al. 1990; Huestis et al. 1992) arrhythmias and ventricular fibrillation (see also NIDA, 2024; Paulraj, 2024). Furthermore as found in my own research (Heishman et al. 1990 and Huestis et al. 1992) plasma THC levels plummet rapidly beginning with minutes following the marijuana vapor/smoke inhalation which means that seemingly low levels of THC exposure from post mortem blood samples can greatly underestimate actual exposure (see also NEW REF COMING).

41. I do not see any basis in the autopsy report or NMS labs assessment of mitragynine or 7-OH levels that suggest anything but relatively low levels as compared to those that are more likely to be associated with death (see Papsun et al. 2023; Henningfield, Grundmann, Huestis and Smith, 2026). The mitragynine level was determined to be 150 ng/mL by NMS Labs and 158 ng/mL by UCSF Clinical Toxicology. NMS did not report 7-OH. UCSF Clinical Toxicology reported 0.8 ng/mL with a footnote indicating the “[v]alue was below the lower limit of quantification of 3 ng/mL and equal to the limit of detection for the analysis.”

42. Huestis et al, 2024 assessed the effects of single and consecutive daily oral ascending doses of dried kratom leaf powder in healthy adults, including the mitragynine and 7-OH concentrations, over 10 days after a single dose and 23 days after multiple dosing. This was a Health Canada approved study designed to detect kratom-related adverse effects. In the trial’s highest dose group (4000mg kratom leaf powder / 53.2mg mitragynine daily for 15 days), the mean steady state peak plasma concentration (C_{max}) measured was 143 ng/mL with a median of 155 ng/mL (range 64.3 – 215 ng/mL). In this same group, the mean 7-OH level measured was 21-8 ng/mL (range 13.3 – 31.7 ng/mL). The study concluded that the kratom powder was well-tolerated with no clinically significant abnormal findings in blood pressure, heart rate, or ECG. No active participants had abnormal QTc intervals, and QTc intervals greater than 500 milliseconds were not reported.

43. Reissig et al., 2024 evaluated the pharmacokinetics, pharmacodynamics, and safety of single ascending oral doses of botanical kratom in non-dependent, recreational polydrug users with opioid experience. In this pilot, placebo-controlled, dose-finding study performed under an Investigational New Drug (IND) application, participants were administered single doses of 1g, 3g, 8g, 10g, or 12g of oral kratom powder in capsules. In the highest dose groups, C_{max} for mitragynine ranged from 250-300 ng/mL but 7-OH levels were below the lower limit of quantitation. The study concluded that at the doses tested, kratom was well-tolerated with no serious adverse effects reported, including no abnormalities in vital signs and ECG.

44. Smith et al., 2024 assessed the acute effects of a “typical” morning dose of kratom in 10 adults who use kratom regularly. This was an observational study designed to measure physiological, subjective, and psychomotor effects and to quantify alkaloids in plasma. Participants self-administered their typical dose of kratom (mean 5.16 g, range 1.1-10.9g). The mean plasma concentration for mitragynine found was 175.6 ng/mL (median 174.5 ng/mL, range 36.6 – 396.5 ng/mL). The mean plasma concentration for 7-OH was 34.0 ng/mL (median 27.4 ng/mL, range 2.9 – 77.7 ng/mL). The study concluded that among these regular consumers, there were “few clinically significant differences” pre- and post-dosing. Physiological changes,

including those in blood pressure and heart rate, were described as “minor” and “not clinically significant.”

45. Each of these studies recorded mitragynine blood concentrations at levels similar or higher than what was found in this case.

46. Taken together, these data from clinical studies, designed to the standards of an FDA registration study for safety (Huestis et al. 2024 and Reissig et al. 2024) observed somewhat higher mitragynine blood concentrations without any evidence of adverse cardiovascular or any other serious adverse effects.

47. The potential dose of mitragynine that would be likely to substantially contribute to or cause death is not known, but Ms. Moller’s documented level appears to have been very low. Additionally, post-mortem testing identified at least two cannabinoids, diphenhydramine, and promethazine. Of course, novel fentanyl related substances and other substances may have been involved but not tested for.

48. Plaintiff contends that powdered kratom products sold in the United States are far more dangerous than other natural products that are sold over the counter. This is an overly broad statement given the diversity of kratom products and natural products that are sold over the counter (OTC). For example, many products based on natural and botanical ingredients carry serious health and in some cases addiction risks, such as caffeine, yohimbine, kava, and green tea extract.

ADDITIONAL EVIDENCE-BASED SUPPORT FOR OPINIONS

Opinion 1: Kratom is not and should not be characterized as “an opioid,” nor regulated as a dangerous or addictive controlled substance in the U.S., CSA or under the International Drug Control Conventions of the United Nations. I agree with the determinations of the DEA and UNODC that kratom does not warrant such designations or control.

49. Kratom is not an opioid or narcotic by nature of its botanical origin, chemical structure or overall pharmacology and thus it is not included in the CSA or any of the United Nations International Drug Control Treaties. Nor has it ever been listed as a national drug threat in DEA’s annual National Drug Threat Assessment reports as necessary to meet statutory requirements for CSA Scheduling. Furthermore, kratom does not produce opioid-like respiratory depressant effects or the powerful euphoria that fuels the opioid epidemic. Its primary alkaloid and metabolites that do have some activity similar to opioids are partial agonists, meaning that their strongest effects are weaker than classic opioids (Henningfield et al. 2018, 2022, 2024; Kruegel et al. 2019; Kruegel et al., 2016; Henningfield and Fant, 2016; Varadi et al. 2016).

50. The DEA, NIDA, the U.S. Assistant Secretary for Health, and the WHO’s Expert Committee on Drug Dependence all agree with the conclusion that kratom is not an “opioid” and should not be scheduled as such.

51. In recent years, the FDA has been reevaluating its 2017 and 2018 statements that had suggested kratom had narcotic opioid-like effects. The FDA’s stated position as of December 2023 was that it “ha[d] not yet made a determination regarding whether kratom is dangerous.” (*United States v. Nine2Five, LLC*, Case No. 3:23-CR-00179-TWR (S.D. Cal.) ECF No. 110-8 at

2.) In February 2024, the FDA also updated its website to state: “In rare cases, deaths have been associated with kratom use, as confirmed by a medical examiner or toxicology reports. However, in these cases, kratom was usually used in combination with other drugs, and the contribution of kratom in the deaths is unclear.” (FDA, Feb. 22, 2024, at <https://www.fda.gov/news-events/public-health-focus/fda-and-kratom>).

52. Although the FDA or DEA theoretically could determine that kratom and its constituents are sufficiently pharmacologically equivalent to previously scheduled drugs such as morphine-like opioids or methamphetamine-like stimulants, the scientific evidence does not support that conclusion. In 2017, the FDA developed an 8-factor analysis to support such a conclusion, but based on limitations in the evidence cited and because the agency ignored key evidence to the contrary, the FDA’s analysis was not considered reliable or valid by leading experts (e.g., Henningfield et al. 2018; US DHHS (Giroir, 2018) or the WHO Expert Committee on Drug Dependence, 2021).

53. Furthermore, in the FDA’s 2017 8-factor analysis, the agency ignored the serious adverse public health consequences of banning kratom and the benefits of keeping kratom available as a path away from opioid overdose. These considerations are a critical part of drug scheduling considered in factors 4, 5 and 6 of CSA 8-factor analysis as noted in DHHS’s review of the FDA’s analysis led by Assistant Secretary Giroir. Dr. Giroir stated, the “FDA’s recommendation was rejected because of embarrassingly poor evidence and data, and a failure to consider overall public health” (Giroir, 2021; and detailed analysis in Giroir, 2018). The DHHS report raised additional concerns, including the risk of precipitating potentially thousands of opioid overdose deaths, deterring kratom users (including pregnant women) from discussing their use with health care providers, the impact of criminalizing millions of U.S. citizens, and impeding further necessary research.

54. Separate from the DHHS report, I earlier led development of the first CSA guided 8-factor analysis to evaluate kratom’s potential for abuse (Pinney Associates, Henningfield and Fant, 2016). In summary, we concluded that factors 4, 5, and 6¹ weighed against scheduling and that there was not sufficient evidence of factors 1-3 or 7 to recommend scheduling. We further concluded that kratom and kratom constituents did not meet the factor 8 standard.

55. When the FDA’s 2017 8-factor analysis became publicly available, I also led a more detailed evaluation of the FDA analysis, along with eleven other leaders in kratom and opioid sciences and abuse potential. Our conclusions are summarized below:

FDA’s 8-Factor Analysis does not constitute a reliable and valid scheduling decision guiding document.

¹ Factors 4, 5 and 6 pertain to whether a substance with potential abuse-related uses poses a national drug threat and might warrant consideration for CSA scheduling. The factors are typically addressed by the DEA, FDA, NIDA, and experts with national survey data and other national monitoring systems. The factors are as follows: Factor 4: its history and current pattern of abuse; Factor 5: the scope, duration, and significance of abuse; and Factor 6: what, if any, risk is there to public health.

FDA clearly did not involve NIDA or kratom science experts, as revealed by its major deficiencies. A 1985 DHHS Memorandum of Understanding, requires NIDA scientific input on FDA led abuse potential assessment evaluations.

The FDA analysis is incomplete, omitting key data sources routinely relied upon for identifying trends in abuse (e.g., the major federal surveys) and key scientific studies, AND is out-of-date as it does not refer to critical studies including those by NIDA (Yue et al., 2018 and Hemby et al., 2018).

The evidence is sufficient to conclude that placement of kratom in Schedule I or any other approach that would ban kratom would lead many kratom consumers to seek black market kratom and some to relapse to opioids and thus pose a serious risk of death (Henningfield et al., 2018).

The 2021 WHO Expert Committee on Drug Dependence came to a similar conclusion.

56. My review has been updated, peer-reviewed and published in 2018, and again in 2023 based on additional research (Henningfield et al. 2018, 2022, *see also* 2024). Those reviews include hundreds of new studies and additional reviews by other kratom research leaders who came to similar conclusions.

57. Kratom is in the same family as coffee, and like its botanical cousin, kratom contains many substances referred to as alkaloids, which tend to be somewhat alkaline and bitter in flavor. More than 40 alkaloids are identified in kratom to date, with most having little or no known pharmacological effect, or occurring at such low levels as to be of little cause for harm or benefit. The main ingredient in kratom currently thought to account for most of the pharmacological effects reported by consumers is mitragynine, which does not have strong rewarding and addictive effects like conventional stimulants, nor respiratory depressant effects like opioids (Brown et al. 2017; Henningfield, Grundmann, Huestis & Smith, 2020; McCurdy et al. 2024).

58. Unsurprisingly, given its botanical origin, kratom leaf products and extracts that contain primarily mitragynine are consumed by many people in place of coffee for alerting and occupational performance enhancing benefits (Henningfield et al. 2024). Another example of the distinction between kratom and narcotic like opioids. The term “narcotic” is derived from the Greek word for “stupor” and used to describing the sedating, sleepiness inducing, and sometimes dulling-of-the-senses effects of opioids.

59. To summarize, available scientific research has determined kratom does not have narcotic opioid-like properties.

Opinion 2: Kratom is not characterized by “high abuse” potential.

60. The FDA has performed an initial study of high doses of kratom without finding serious adverse effects and with affirmative findings that the study established that the products were sufficiently safe to pursue further such high dose research (Reissig *et al.* 2024).

61. The abuse potential reviews and specific studies cited for Opinion 1, including several hundred basic pharmacology, animal and human studies as well as extensive surveillance and epidemiological research, also support Opinion 2. The vast majority of this research has been conducted by highly acclaimed researchers at leading research institutions and with support from NIDA.

62. Recent peer-reviewed articles that address this include Henningfield et al. 2022 and 2024. Additionally, several studies funded by NIDA and conducted by NIDA and Johns Hopkins researchers using state of the art monitoring and study approaches have found that for most kratom consumers who show some signs of dependence or withdrawal, the symptom and harm profile was generally more similar to caffeine than opioids, methamphetamine or alcohol with respect to severity and self-manageability. The studies also found that kratom consumers, like caffeine consumers, are more likely to report that kratom is beneficial in daily life, functionality, and with respect to managing pain, stress, anxiety, insomnia, and withdrawal from opioids and other drugs (Grundmann, Green, Berthold et al. 2025; Henningfield et al. 2022; Smith, Panlilio, Feldman et al. 2024; Smith, Rogers, Sharma et al. 2023, Swogger, Smith, Garcea-Romeu et al. 2022).

63. Taken together, the current scientific studies and reviews show that people who report any signs of kratom dependence or “addiction” generally have few symptoms. Additionally, the reported symptoms were generally related to patterns of use (e.g., using more over time and using longer than originally intended) instead of the more severe and disruptive symptoms common with opioids and methamphetamine-like stimulants.

Opinion 3: Kratom does not carry a high risk of death. To the contrary, the risk of death by kratom alone appears very low and rare.

64. This has been known for decades in Southeast Asia, where kratom is likely used daily by more than 100 million people and has been studied for decades. Unfortunately, FDA’s earlier mischaracterization of kratom as a “narcotic opioid” was accepted by much of the popular media, by some prestigious medical institutions such as the Mayo Clinic, and apparently by many medical examiners who seemed to assume that if kratom was present in an overdose case, it could be listed as a cause of death. They would claim that “lethal” doses were taken, despite the fact that a lethal dose has not been determined. Typically, the determination that kratom was the cause or contributing factor in a death is based on the absence of evidence of other substances, even though oftentimes there was no testing done to detect the presence of several potentially lethal substances.

65. I led a peer-reviewed published evaluation cited by NIDA and others that concluded the risk of death involving kratom was at least one thousand times less than that posed by opioids. Perhaps more important are the conclusions of NIDA nearly a decade ago and revised slightly with increased nuance in 2022 (see below), along with DEA’s approach since 2016.

66. NIDA’s statements related to kratom’s risk of death on its kratom Science Facts Webpage in February 2016 were as follows: “Kratom by itself is not associated with fatal overdose, but commercial forms of the drug are sometimes laced with other compounds that have caused deaths.”

67. NIDA's webpage was updated in March 2022 to state:

A very small number of deaths have been linked to kratom products compared to deaths from other drugs. While more research is needed, it appears that fatal overdose from kratom use alone is extremely rare. A 2019 report found that 11 deaths between 2011 and 2017 in the United States were associated with kratom exposure, including two deaths associated with kratom exposure alone. In contrast, during that same period, more than 200,000 people died from opioid-related overdose.

68. With the exception of its August 2016 FDA-recommended proposal for temporary placement in Schedule 1 of the CSA, the DEA has not concluded that kratom poses a substantial risk of death or poses a national drug threat. The DEA's "Kratom Drug Fact Sheet" webpage includes the following based on user reports and available data (DEA, 2020, April at https://www.dea.gov/sites/default/files/2020-06/Kratom-2020_0.pdf):

What are the effects?

At low doses, kratom produces stimulant effects with users reporting increased alertness, physical energy, and talkativeness. At high doses, users experience sedative effects. Kratom consumption can lead to addiction. Several cases of psychosis resulting from use of kratom have been reported, where individuals addicted to kratom exhibited psychotic symptoms, including hallucinations, delusion, and confusion.

What does it do to the body?

Kratom's effects on the body include nausea, itching, sweating, dry mouth, constipation, increased urination, tachycardia, vomiting, drowsiness, and loss of appetite. Users of kratom have also experienced anorexia, weight loss, insomnia, hepatotoxicity, seizure, and hallucinations.

69. The DEA broadly uses the term "abuse" for use of any substance with psychoactive effects that has not been approved by the FDA for therapeutic use as a drug. FDA approval has generally been the operational standard for what is termed Commonly Accepted Medical Use (CAMU) in the CSA. In contrast to DEA's Kratom Drug Fact Sheet, its Narcotic/Opioid Drug Fact Sheet states the following with respect to effects: "Overdoses of narcotics are not uncommon and can be fatal." (See DEA 2020, April at <https://www.dea.gov/sites/default/files/2020-06/Narcotics-2020.pdf>).

70. Additionally, reports that a condition or event was associated with kratom use, such as DEA and FDA reports of kratom-associated "hepatotoxicity" and "seizures," do not mean that kratom has conclusively been determined to be the actual cause. For example, liver disease can have many contributors, including acetaminophen, alcohol, viral infections, obesity, diabetes, and genetic disorders. Similarly, neurological disorders and brain injuries can be associated with falls, vehicular accidents, concussions, genetic conditions, viral infections, alcohol, other substances of abuse, medications commonly used to treat anxiety and depression, sleep deprivation, discontinuation of certain medicines, and flashing lights. The foregoing opinion is based on my

experience working with medical practitioners to develop medicines for treating seizure disorders and to determine if rarely observed associated events should be included in warnings for drugs that carry known risks of seizure and liver disorders.

71. FDA's 2017-2018 public kratom communications did not draw the distinction between kratom and narcotics that has long been well understood by FDA and NIDA.

72. Whereas narcotic opioids account for most of the nearly 90,000 documented deaths that are widely agreed by the DEA, FDA, NIDA, and CDC to be primarily caused by drugs of abuse (NIDA, 2024), it is not clear how many, if any, can be primarily, if at all, attributed to kratom (*see* current FDA and NIDA, kratom webpages and Henningfield et al. 2022 & 2024).

73. The challenges in determining causality of a substance for injury and death are difficult for many substances, and in cases involving prior or existing medical conditions and other substance use, virtually impossible to definitively confirm. For example, although caffeine may cause an overdose death at extraordinarily high doses, it is rare even at that high dose to carry overdose risk (Murray and Traylor, 2025).

74. Similarly, tetrahydrocannabinol (THC), the primary active constituent in cannabis, is presumed to be able to cause or contribute to lethality at some undetermined dose (Turner et al. 2023). As with kratom, overdose death in cannabis users in which there is no evidence of other substances or other potentially lethal conditions are rare.

75. For substances such as kratom with a low risk of overdose death, it may be practically impossible to determine whether a single substance is the cause of death or can be eliminated as a theoretical cause of death. From a public health perspective, it is more likely that kratom is contributing to reduced drug overdose-related deaths than contributing to deaths. The most recent drug overdose data revealed a decrease in estimated drug overdose deaths in 2024 as compared to 2023, with synthetic opioids (fentanyl and related substances) accounting for 48,422; psychostimulants (including methamphetamine) accounting for 29,456 and cocaine accounting for 22,174. Kratom was not listed as a cause of death in these or any earlier CDC and NIDA estimates (CDC, May 14, 2025, media release). Although the downward trends are under investigation by CDC and NIDA, federal officials (e.g., NIDA Director Nora Volkow at the 2024 June Annual Meeting of the College on Problems of Drug Dependence) believe that harm reduction efforts, including increased access to naloxone and needle exchange, and harm reduction treatment efforts including substitute opioids such as methadone and buprenorphine contributed to the reductions. This contradicts the theory that kratom is fueling the overdose epidemic because the prevalence of kratom use appears to have increased. For example, a 2025 publication of a nationally representative survey suggests that the prevalence of past 30-day kratom use among adults is 9.1%, which suggests more than 20 million people in 2024 consumed kratom (Grundmann et al. 2025).

76. In my opinion, there is strong evidence that the use of kratom as a harm reduction approach by people who are addicted to opioids has contributed to the apparent downturn in drug overdose deaths; however, the magnitude of this likely public health benefit of kratom is not known. My opinion on the likely net public health benefit provided by licit retail access to kratom across most of the United States is also supported by nearly a decade of comments of kratom consumers to federal agencies, as well as in public hearings on kratom regulatory needs that I have

participated in. It is also supported by several peer-reviewed and published scientific surveys, including one of my own (Coe et al. 2019), which suggests that many thousands of people who had been using and in some cases were addicted to opioids reduced or eliminated their use of opioids through their consumption of kratom (Coe, et al. 2019; Garcia, 2020; Grundmann, 2017, Grundmann et al. 2025; Henningfield et al. 2016, 2018, 2022; 2024; Smith, Panlilio, Feldman et al. 2024).

77. This is also consistent with the summary of findings of the National Institute of Drug Abuse “that people report using kratom to alleviate pain, to address symptoms of mental health conditions like anxiety and depression, to help stop or reduce opioid or other substance use and to manage withdrawal symptoms and cravings related to opioids and other drugs. Most report multiple reasons for using kratom.” (NIDA, 2022).

78. It was for those same reasons that in 2018, the Assistant Secretary for Health Admiral Giroir rescinded FDA’s effort to end the legal distribution, sale, possession and use of kratom by making it a Schedule I substance in the Controlled Substances Act as I discuss in this report. In the rescission letter and following Twitter comment, he made clear that the evidence did not support the conclusion that kratom itself caused overdose deaths or contributed to the opioid epidemic and that, to the contrary, thousands of people might die from drug overdose if kratom’s sale was prohibited (Giroir, 2018, 2020).

Opinion 4: There is no consensus on the basis by which kratom might cause death.

79. The evidence for this opinion is largely summarized above. Additionally, in contrast to most substances that contribute to the U.S. drug overdose epidemic, there is no consensus on the manner by which kratom might cause death. In many cases for which death is attributed to kratom, no actual cause was put forward other than “intoxication,” “consumption,” or a measured mitragynine blood level.

80. This is in contrast to most of the substances that contribute to overdose deaths, e.g., respiratory depression by opioids and sedatives, cardiovascular causes by stimulants. The few deaths that involve kratom are rare, idiosyncratic, and in most cases involve other substances and/or disease conditions making it virtually impossible to rule in or rule out the potential contribution, if any, of kratom.

81. This opinion has been extensively supported by numerous studies, including nearly 200 cited in my peer-reviewed 2024 article entitled, “Kratom safety and toxicology in the public health context: research needs to better inform regulation.” It was coauthored with three other leading kratom and toxicology researchers: Drs. Grundmann, Huestis and Smith.

82. Harmony Moller appears to have suffered from cardiovascular disease, and several drugs were identified in post-mortem blood samples. The basis for concluding that her death resulted from use of a kratom product is not clear.

83. Virtually any consumable substance that is necessary for life, such as water and oxygen, most marketed food products and dietary supplements, and FDA approved medicines that are presumed to be “safe” carry risks if used at excessive levels. It is misleading to imply that such substances are generally dangerous or that any substance that can cause injury at extremely high

levels of intake should be considered dangerous and not used or marketed. This is fundamental in toxicology and best summarized by the following version of Paracelsus 16th century dictum: “the dose makes the poison” and its corollary “the dose makes the medicine.” As discussed in this opinion and in many peer-reviewed study publications and reviews of such (e.g., Henningfield, et al. 2022, 2024; McCurdy, et al., 2024), many studies over decades have documented that kratom and its most abundant neurobiologically active constituent, mitragynine, are primarily used for their effects that are considered beneficial to many people and traditional health practitioners in the U.S. and Southeast Asia.

Opinion 5: There is no consensus as to what level of kratom consumption or constituent level in the bloodstream would constitute a lethal dose.

84. A frequently cited source for establishing a lethal dose of mitragynine in humans is Papsun et al. (2023). What Papsun actually concluded is that “blood mitragynine concentrations of > 1000 ng/mL are more often *associated with* severe adverse events, up to and including death”—not that 1000 ng/mL was a known harmful or lethal dose (Papsun et al., 2023) (emphasis added).

85. Most medical examiner reports that I have reviewed in which a causal role for kratom was suggested have either based their conclusions on levels of mitragynine in the blood (despite the fact that no level has ever been determined as a lethal dose), or on other medical conditions that may have been part of the decedent’s medical history (e.g., seizures). Additionally, in these cases the decedent may have a history of use of substances that carry risks of liver, cardiovascular, or seizure disorders, or the decedent may have been using other drugs for which they were not tested.

86. For many drugs and substances, such as opioids, stimulants, sedatives, alcohol, and caffeine, there is reliable evidence-based estimates of what constitutes a lethal dose. This is sometimes referred to as the LD50 or dose at which 50% of animals and possibly humans might die. The reliability of the estimates varies across drugs but for opioids, sedatives and alcohol, the findings are considered reliable.

87. Theoretically, most any substance, including water, can be lethal at a high enough intake. However, a lethal level has yet to be determined for kratom despite many years of effort. The lethality of kratom is so low that the many animal studies that have attempted to determine the lethal dose of kratom solutions or kratom’s primary active ingredient, mitragynine, have failed to produce death (Henningfield Grundmann, Huestis and Smith, 2024; Henningfield Rodricks et al. 2022b).

88. The FDA’s recommended respiratory effect study protocol (Xu et al. 2020, 2021) was applied to determine the potential life-threatening and lethal doses of kratom. Although numerous studies previously evaluated respiratory and potentially life-threatening effects of mitragynine and kratom extracts in numerous animal species (mouse, rat, dog, monkey), none had employed FDA’s recommended approach.

89. I, along with Drs. Marilyn Huestis and Joseph Rodricks, as well as Dr. Aaron Magnuson, conducted a study meeting the FDA's recommended respiratory effect study protocol for evaluating respiratory safety of opioids and other drugs (Xu et al. 2020, 2022).

90. The study had a challenging adaptive design that pushed the dose to the highest physiochemical feasibility or until the point of life-threatening effects. Mitragynine doses were systematically increased to the maximum level that could be administered—400 milligrams per kilogram (mg/kg)—which was higher than that achieved in most other animal safety studies.

91. The tested mitragynine doses were 20, 40, 80, 240, and 400 mg/kg, which are equivalent to approximately 3.2, 6.6, 12.9, 38.7, and 64.5, (mg/kg) respectively when converted to human equivalent doses (Nair and Jacob 2016). These mitragynine doses produced peak ("C_{max}") median blood plasma levels of 723, 1720, 2497, 5182, and 7513 (with levels as high as 10,096). In contrast, it appears that many daily kratom consumers ingest less than 1 mg/kg, with other more heavy users consuming a few mg/kg over the course of a day. Typical human consumption levels are far lower than those evaluated in numerous animal studies in multiple species routinely used to evaluate drug and dietary safety for FDA submissions (Henningfield et al. 2022; 2023, 2024).

92. In this study, the FDA comparator opioid (oxycodone) doses produced striking dose related behavioral and life-threatening effects, including plummeting blood oxygen levels and deaths at the two highest doses. In contrast, mitragynine produced no life-threatening effects and no dose or time-related respiratory gas parameters recommended by the FDA. The two highest doses produced dose-related increases in expected effects, such as transient disrupted mobility. There were no dose or time related effects on the respiratory gas measures that would suggest adverse respiratory effects or risk of overdose death. These data are consistent with findings by other investigators using other techniques of respiratory assessment, though most of those studies did not achieve the highest dose level that was administered in our study (e.g., Hill et al., 2022; Macko et al. 1972, Hill et al. 2022, Váradi et al., 2016; and other studies review by the forgoing investigators and by Henningfield et al. 2022, 2024).

93. There are no human studies or data that provide a basis for determining the dose at which mitragynine, or any other kratom associated alkaloid, or whole kratom leaf material or extracts might produce life threatening cardiovascular or respiratory or other effects. Nor have any of the many animal studies that have attempted to achieve potential life-threatening effects determined what might constitute a life-threatening or lethal dose. Thus, medical examiner reports stating that a decedent had a lethal dose or that kratom was the cause of death are not supported by scientific evidence and are in fact contradictory to scientific evidence.

94. In addition to the dose of various potentially harmful constituents in a substance or product are the many other aspects of widely consumable products that may contribute to their effects, desired and undesired. This is true with respect to food such as wheat, cheese, meat, nuts and vegetables, which may be beneficial in many people, harmful to some depending on individual factors including allergies, and depending how the products were obtained, processed for use, packaged and other factors that may affect their safety due to contamination with heavy metals, harmful bacteria and other substances.

95. It is well established that marketed kratom products vary widely in their purity and levels of contaminants in the United States. For example, Prozialeck et al. (2020) found that kratom products purchased in stores in 2019 before product purity testing was becoming more common by marketers varied widely in contaminants.

96. Generalizing from reports of harm associated with kratom that have been documented across the nation with diverse products to the Defendants' products ignores the reality that kratom products vary widely in their ingredients and associated risks of harm and benefit. For example, some products marketed as "kratom" and as "derivatives of kratom" actually contain high doses of the mitragynine metabolite 7-OH, which is not generally present at neurobiologically meaningful levels in natural leaf product but can be synthesized from naturally occurring mitragynine to form 'semi-synthetic' 7-OH. This is thought to carry higher risks of adverse effects than kratom leaf-based product (Smith et al., 2025). Thus, reports by consumers of adverse effects associated with the use of products with high levels of 7-OH as due to kratom are misleading and should not be referred to as due to "kratom". Semi-synthetic metabolites of mitragynine are not kratom.

97. For example, Smith et al. (2025, p. 387), concluded as follows: "To be clear: equating 7-hydroxymitragynine products to kratom is analogous to equating synthetic cannabinoids to unaltered cannabis or hemp. Although not all organic kratom products are equal, they have not emerged as a net detriment to public health, and they remain unscheduled at the federal level. Novel semi-synthetic 7-hydroxymitragynine products pose public health risks due to the unknown chemical constituents and the known pharmacology of 7-hydroxymitragynine. Clinicians must screen patients for their use and policymakers must distinguish between kratom and 7-hydroxymitragynine."

98. The advice offered by Smith et al., which I agree with, is not generally followed and even national surveillance systems such as America's Poison Control Centers and the FDA Adverse Events Reporting System (FAERS), which document "kratom" reports do not and cannot reliably differentiate between reports from consumers and health professionals that involved pure kratom versus reports by consumers who, perhaps unknowingly, had consumed products containing high levels of 7-OH. I discuss this issue in the context of FDA's July 29, 2025, media release addressing 7-OH at the end of this report (FDA, 2025a, b, c, d).

99. Plaintiffs appear to have made no distinction between the vast range of products marketed in the U.S. and on the internet, which is known to include contaminated and adulterated products as compared to products that are made with high quality kratom leaves that have been tested to determine their purity and then manufactured and packaged so as to minimize contamination as is the case with O.P.M.S. and many other products. Natural kratom leaf-based products that are not adulterated with toxic substances or artificially high levels of alkaloids such as 7-OH do not carry serious risk and dangers based on decades of use in the United States and centuries of use in Southeast Asia (Henningfield et al. 2024; Grundmann et al. 2024; Smith et al. 2025).

Opinion 6: Kratom is an overall public health asset that is used by many people as a harm reduction approach to reduce or eliminate the use of opioids, sedatives, stimulants, and alcohol. Such public health benefits were considered in the determinations of the DEA, the

DHHS, and the WHO Expert Committee on Drug Dependence to not restrict access of kratom by controlled substance scheduling.

100. The “kratom 8-factor analysis” contained in Henningfield and Fant, 2016, which I led and which was submitted to the DEA in response to its request for comments in its October 2016 Withdrawal of Notice of Intent to Temporarily Place Mitragynine and 7-Hydroxymitragynine Into Schedule I (DEA, 2016b), supports this opinion. Our analysis followed the format of the CSA 8-factor analysis of pharmacology and public health data from more than 100 scientific publications, major federal surveys used to evaluate public health effects of substance use, two national kratom-focused surveys, more than 1000 testimonials, and discussions with other kratom experts. This report was submitted to the DEA, FDA and NIDA, and hundreds of more recent studies have confirmed its core conclusions, including conclusions 4 through 7 related to public health set forth below:

Factor #4: Kratom consumption is widespread across the U.S. and spans more than two decades, but kratom consumption has not emerged as a substance abuse problem in the U.S. as measured by any of the U.S. national substance abuse monitoring surveillance systems or by our nation’s networks of substance abuse treatment programs that are constantly adapting to the challenges posed by those seeking treatment for emerging forms of abuse and dependence.

Factor #5: Current kratom users report being likely to be adversely affected and possibly motivated to seek illicit sources if lawfully marketed kratom were no longer available. This would seem likely to include many Southeast Asian immigrants who are believed to have brought kratom consumption customs with them to the U.S.; however, there has been very little documentation and characterization of kratom use patterns in the U.S. by such populations.

Factor #6: Kratom consumption appears to be primarily motivated by its perceived effects that enhance well-being, occupational performance, and social interactions, as well as serving as a natural “home remedy” that is preferred by millions of Americans to conventional medicines.

Factor #7: The foregoing is consistent with the pharmacology of kratom and more specifically its alkaloids (MG and 7-OH-MG), which produce mixed pharmacological effects that are generally mild and caffeine stimulant-like at lower dosages. Consumption does not typically interfere with work or social activities and commitments, and in fact kratom is widely reported in the U.S., as in Southeast Asia, to contribute to work productivity, quality of life, and social relationships.

101. My major conclusions in 2016 and today are consistent with the tweet response of Assistant Secretary Dr. Giroir to the FDA commissioner, who led the DHHS review of the FDA’s prior approach characterizing kratom as a narcotic-like opioid:

May 21 2021 Dr. Giroir responds to Dr Gottlieb
Kratom Tweet



102. In its review and formal order to rescind the February 2018 scheduling request, the DHHS made clear that (a) the evidence did not support scheduling and did not meet the statutory requirements for scheduling, and (b) the main public health threat was not kratom use but a kratom ban that could foreseeably include the following:

Furthermore, there is a significant risk of immediate adverse public health consequences for potentially millions of users if *kratom* or its components are included in Schedule I, such as:

- Suffering with intractable pain;
- *Kratom* users switching to highly lethal opioids, including potent and deadly prescription opioids, heroin, and/or fentanyl, risking thousands of deaths from overdoses and infectious diseases associated with IV drug use;
- Inhibition of patients discussing *kratom* use with their primary care physicians leading to more harm, and enhancement of stigma thereby decreasing desire for treatment, because of individual users now being guilty of a crime by virtue of their possession or use of *kratom*
- The stifling effect of classification in Schedule I on critical research needed on the complex and potentially useful chemistry of components of *kratom*.

Therefore, I conclude at the current time, available evidence does not support mitragynine and 7-hydroxymitragynine being controlled in Schedule I of the Controlled Substances Act. This assessment supersedes the previous recommendation letter from Acting Assistant Secretary Wright dated October 17, 2017. In the meantime, it is recognized that *kratom* may potentially have harmful effects, especially in specific circumstances and/or when used with potent prescription or illicit drugs.

(Giroir, 2018 August kratom scheduling rescission order letter to the U.S. Department of Justice, DEA Administrator Dhillon).

Opinion 7: Most people use kratom for health and well-being, including as a supplement to or replacement for caffeinated beverages, and to self-manage depression, anxiety, pain, opioid and other drug withdrawal. Like many dietary substances that consumers use, the health and well-being benefits of kratom are not and cannot be approved for therapeutic use by the FDA.

103. My opinions related to the reasons people use kratom are based on decades of study in Southeast Asia and more than a decade of study in the U.S. Research has been rapidly increasing in the U.S. over the past decade and has been primarily supported by the NIH, led considerably by NIDA, with encouragement of such research and funding from Congress. For example, the Fiscal Year 2023 Omnibus bill included the statement that “[NIDA supported research on kratom] may

provide help for some Americans struggling with addictions, given its analgesic and less addictive properties as compared to opioids.” (<https://www.congress.gov/congressional-report/117th-congress/house-report/403/1>).

104. The scientific evidence for my conclusions related to primarily beneficial use is strong and widely replicated in various peer-reviewed studies in the U.S. and Southeast Asia and is summarized at NIDA’s kratom science website. This evidence includes surveys that suggest most of the several million U.S. kratom consumers find kratom more effective, tolerable, accessible, affordable, or simply desirable because of their preferences for natural products than prescription drugs and FDA-approved over-the-counter medicines. This is despite the fact that kratom, as is the case with most dietary and natural products, is not approved for therapeutic use by the FDA.

105. This opinion is extensively supported by numerous studies in Southeast Asia and many more in the U.S., including those conducted by NIDA researchers led by Dr. Kirsten Smith and others and in reviews by global kratom research leaders such as Prozialeck et al. 2019. Key surveys include Coe et al., 2019; Garcia-Romeu et al. 2020, Grundmann et al. 2017. (*See also* review by Henningfield et al. 2023, 2024 and several more from 2020 to 2025 by Dr. Smith et al.).

106. Together, these studies show that kratom is diversely used, primarily by adults, especially among those aged 35-55, with jobs and health insurance. Participants report that their consumption is primarily for health and well-being. This includes consumption as an alternative to caffeinated products for alertness and increased focus, for the self-management of pain, and to improve mood. Many consumers state that kratom worked better for them and had fewer side-effects than the FDA-approved medicines they had taken, and/or that they preferred natural products.

107. A smaller but important fraction of consumers are people who consider kratom as a “lifeline” or a path away from opioids. They use kratom to manage opioid withdrawal and reduce or eliminate opioid use. Some report use of kratom to reduce or cease use of alcohol and stimulants such as methamphetamine and cocaine, which is consistent with its diverse effects that include stimulation and relaxation. Addiction to kratom is reported by some but generally a small minority of respondents in major published surveys and with characteristics that appear relatively benign and not problematic as compared to opioids and other prototypic substances of abuse.

108. Recent research led by Dr. Kirsten Smith, in collaboration with NIDA and Johns Hopkins colleagues, has found that many people use kratom for multiple reasons that may evolve, e.g., first to escape opioid use, and later for improved general health and well-being. Her studies also demonstrate that among people who might meet criteria for a “kratom use disorder” (also known as “dependence” and “addiction”), in contrast to use disorders with opioids, stimulants, and alcohol, use of kratom is generally relatively benign in that it does not interfere with social and occupational commitments and is not harmful in its own right but may involve craving and regular use.

109. Similar to Dr. Smith’s research, Dr. Garcia-Romeu et al. (2020) concluded: “This study supports the results of previous studies (Coe et al., 2019; Grundmann, 2017; Smith and Lawson, 2017; Swogger et al., 2015) by suggesting that kratom has a relatively benign risk profile

with only a minority of respondents endorsing kratom related adverse effects, withdrawal symptoms, or problematic use.”

Opinion 8: Kratom is legal federally and is also a legally marketed product in 44 states. (Henningfield et al. 7-OH Eight Factor Analysis, September 2025).

110. DEA, FDA, and NIDA positions in recent years are similar to mine in these respects.

111. For example, the DEA² states as follows on its webpage:

What is its legal status?

Kratom is not controlled under the Controlled Substances Act; however, there may be some state regulations or prohibitions against the possession and use of kratom. The FDA has not approved Kratom for any medical use. In addition, DEA has listed kratom as a Drug and Chemical of Concern (DEA, 2020 Kratom Drug Fact Sheet).

112. Several of the six states that placed kratom as a Schedule I drug in their state Controlled Substances Act frameworks on advice from FDA from 2014 to 2016 are in the process of replacing those laws with laws to ensure legal access and appropriate regulatory oversight of kratom.³ The reason that FDA encouraged states to place kratom (specifically, mitragynine and 7-hydroxymitragynine) in Schedule I of the Controlled Substances Act and requested that DEA take this action as well is because kratom could legally be sold as a unique type of food and thus, did not require premarket “approval” to be marketed, sold, possessed or consumed. This is consistent with its regulatory place as a dietary ingredient as defined in the United States Code, Title 21-FOOD AND DRUGS, Chapter 9 Federal Food Drug and Cosmetic Act Subchapter Definitions (U.S.C § 321). Kratom is not an approved prescription or over-the-counter drug, nor could it be because it is not a drug product. When some companies have made what FDA considers to be drug product claims, FDA has warned them to not make those claims. The FDA’s Office of Dietary Supplement has worked with sponsors and advised them on aspects of their submissions to FDA as New Dietary Ingredient Notifications (NDINs); however, it has claimed deficiencies in the submissions that must be addressed before FDA will accept them. Nonetheless, such products can be and are lawfully distributed, sold, purchased, possessed, and consumed except in states that do not prohibit sales.

113. In contravention of the scientifically justified approach of the federal government and most states, in 2025 the Louisiana legislature passed a law that bans kratom by listing both mitragynine and 7-OH as Schedule I controlled substances. Although the federal government has expressed an intent to list concentrated 7-OH products in Schedule I – an action that I support on

² DEA is in the Department of Justice and is accepted as the highest authority among these agencies pertaining to legal matters.

³ *United States v. Nine2Five, LLC*, Case No. 3:23-CR-00179-TWR (S.D. Cal.).

the basis of the evidence including public health benefits (of keeping kratom and mitragynine legal, and 7-OH in Schedule I) – the federal government has not scheduled mitragynine.

Opinion 9: Kratom carries a low risk of inducing a condition requiring medical care, and the most common side effects (such as gastrointestinal upset) self-resolve and are avoided by consuming less kratom. (Brown et al. 2017; Henningfield Grundmann Huestis Smith, 2024; Swogger et al. 2022). Serious medical conditions reported in kratom users occur at such low rates and so frequently in the context of preexisting conditions or other substance use that determining whether or not kratom consumption was a contributing factor with reasonable scientific certainty is complicated if not impossible.

114. Among the most common undesirable effects reported following kratom consumption are gastrointestinal upset and nausea that generally self-resolve and are avoided by using less kratom.

115. Many of the purported risks of kratom have not actually been demonstrated to be caused by kratom consumption. They are based on consumer and medical reports of association with little evidence to confirm any causal relationship between kratom consumption and the effects reported.

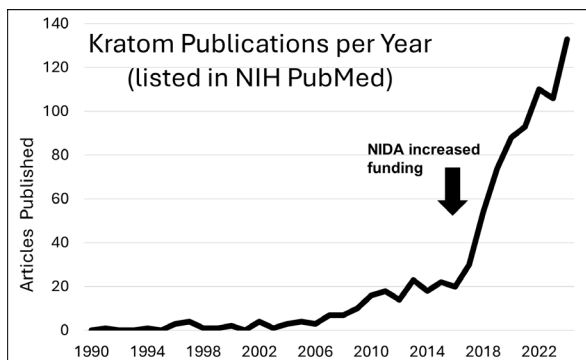
Opinion 10: The vast majority of the evidence upon which I base my opinions was generated by independent researchers primarily supported by the NIH and NIDA and not commercial kratom product developers or kratom advocacy organizations such as the American Kratom Association.

116. Studies of kratom pharmacology, toxicology, safety mechanisms of action and real-world reasons for use and patterns of use are being published at an increasing rate. Around 2015, NIDA funding increased substantially both to address public and regulatory questions and because kratom and its alkaloids showed considerable promise for safer and less addictive products for treating addiction and other disorders. By 2024, the publication rate accelerated to nearly 140 publications per year as based on NIH PubMed listed articles.

117. The rate of publication will likely increase due to ongoing kratom research at leading biomedical research institutions including NIDA's Intramural Research Program, Johns Hopkins University School of Medicine, and the University of Florida. Most of these studies are funded by NIH, NIDA or by government-funded research in other countries, including the Centre for Drug Research University Sains, Malaysia. NIDA supported research has rapidly and substantially expanded the base of reliable and validated evidence relevant to understanding why and how people use kratom, their reasons for use, and the health-related consequences of such use.

118. The vast majority of the scientific studies and publications are not supported by either commercial interests or the AKA. The AKA has supported only one major study of which I am aware, and that was the FDA-recommended study model for evaluating respiratory effects and safety that I led. That funding was unrestricted with no input from AKA in the design, interpretation or publication of the result (Henningfield Rodricks, Aaronson & Huestis, 2023). Only a small percentage of the increased kratom research and publications have been commercially supported.

119. The figure below shows the dramatic increase in kratom scientific publications.



120. These results are from a search of the National Library of Medicine’s PubMed® database of scientific literature published between the dates of 1/1/1990 to 12/12/2024 using the keywords (“kratom” OR “ketum” OR “mitragynine” OR “mitragyna speciosa” OR “7-Hydroxymitragynine” OR “7-OH-mitragynine” OR “7OHMG” OR “7-OH-MG”). Available at <https://pubmed.ncbi.nlm.nih.gov/>.

Opinion 11: The FDA has fueled misunderstandings related to kratom safety, legal status, and benefits by its approach from 2014 to 2018 that was intended to prohibit legal kratom access and criminalize kratom marketing and consumption. More recently, the FDA has ceased making statements that imply kratom has narcotic like risks of addiction and death. However, the FDA’s website at the time of this writing is confusing in its description about kratom’s safety and regulatory status.

121. Despite the FDA’s acknowledgment that kratom associated death are rare, its present website does not include that acknowledgment. Instead, the FDA lists potential adverse effects that have been reported without any effort to discuss which, if any, it has determined should be included on product warning labels. Developing warnings for products in which serious risks are rare is challenging, but the FDA has considerable experience in assessing the evidence and striking the right balance in the interest of public health.

122. Since the formal DHHS kratom scheduling rescission order to the FDA in August 2018, the FDA has not recommended that the DEA schedule kratom in the CSA. As discussed below, the FDA has taken some actions to protect public health as discussed on its FDA and Kratom website.

123. For example, the FDA has issued warning letters to kratom marketers that it has determined made unsubstantiated drug claims or whose products constitute “adulterated products” and has taken other oversight actions. The FDA and the Department of Justice also occasionally “seize” kratom products and imported kratom about which the agencies have concerns or believe pose potential violations. In some cases, these products and shipments are released back to the kratom importers/vendors, who are then allowed to sell the products or the manufactured derivatives of the products after it was determined they do not pose concerns.

124. Unfortunately, the FDA has not announced public hearings or the sort of federal rule making process for kratom that it frequently uses to obtain the latest scientific information for all interested stakeholders. Instead, the FDA continues to state concerns about kratom without developing the evidence base to guide product standards, labeling, warnings, and other approaches to protect public health. At the state level, more than a dozen states have passed laws to ensure access to kratom and protect consumers, including providing guidance on labeling standards and alkaloid content.

125. The current regulatory and policy approaches to kratom ensure legal consumer access along with oversight and research by the DEA, FDA, and NIDA. This includes the following facts:

126. Kratom is legal in most other states and was legal in Louisiana until August, 2025. As announced by the Department of Revenue on July 31 ([at https://revenue.louisiana.gov/news-and-announcements/2025/new-penalties-for-kratom-in-effect-aug-1/](https://revenue.louisiana.gov/news-and-announcements/2025/new-penalties-for-kratom-in-effect-aug-1/)), “Starting Aug. 1, 2025, severe new penalties are in effect for the possession of the herbal supplement known as Kratom. Kratom is sold often as an energy booster, pain reliever and mood lifter. Its potential harmful side effects include liver toxicity, seizures and death.”

127. According to Act 41 of the 2025 Regular Session of the Louisiana Legislature, it is unlawful for any person in Louisiana to knowingly or intentionally produce, manufacture, distribute, dispense or possess kratom.

128. Depending on the amount of kratom involved, offenders may face up to five years in prison and fines of up to \$50,000.

129. Additionally, establishments licensed by the Louisiana Office of Alcohol and Tobacco Control (ATC) are prohibited from selling or storing kratom products on their premises. I note that this law is not consistent with the science or actions or position of the federal government since 2018.

130. Congress has encouraged ensuring kratom access to consumers, increased research, and balanced FDA regulation including the earlier mentioned Fiscal Year 2023 Omnibus bill that included the statement that “[NIDA supported research] may provide help for some Americans struggling with addictions, given its analgesic and less addictive properties as compared to opioids” (at <https://www.whitehouse.gov/briefing-room/legislation/2022/12/29/bill-signed-h-r-2617/>).

131. The FDA no longer makes any statements on its website suggesting that kratom is a narcotic like addictive substance or that it should be banned. However, by refusing to accept kratom as a legitimate dietary supplement or ingredient, refusing to ban kratom, and also refusing to set product standards or labeling requirements, the FDA sows confusion for kratom consumers, manufacturers and sellers.

132. The following is from the FDA’s current (June 13, 2025) kratom webpage⁴:

⁴ <https://www.fda.gov/news-events/public-health-focus/fda-and-kratom>.

How is FDA protecting the public from the risks of kratom?

There are no FDA approved kratom drug products or over the counter drugs containing kratom, or its ingredients- mitragynine, or 7-OH-mitragynine that are legally on the market in the U.S. FDA continues to warn consumers not to use kratom because of the risk of serious adverse events, including liver toxicity, seizures, and substance use disorder (SUD).

Consistent with its mission to protect the public's health, FDA regularly exercises its authority to protect consumers from companies selling unapproved kratom drug products, making false or misleading claims about unproven benefits of kratom, and selling unlawfully marketed kratom dietary supplements and conventional foods. The agency has partnered with the U.S. Customs and Border Protection and with the Department of Justice to take numerous actions to limit the sale of unlawful kratom products in the U.S. The agency continues to work with its federal partners to warn the public about risks associated with use of kratom.

Unapproved drug products are some of the most challenging products that FDA regulates, due to the complex and fragmented supply chain of distributors, wholesalers, retailers, and even individuals. These entities are not usually registered with FDA, may operate out of residences, and distribute kratom through sales made on the internet, social media, smoke/vape shops, other small stores, or by using the mail or other package delivery services. Kratom-containing drug products have been shipped through U.S. and international mail facilities and may falsely be declared as other items, such as potpourri or incense.

FDA will continue to work with its federal partners to warn the public about the risks associated with the use of kratom and protect consumers from entities that are selling violative kratom products, including products with false or misleading labeling claims about unproven health benefits of kratom. Additionally, states may have their own regulations or prohibitions for kratom, mitragynine, or 7-OH-mitragynine products. State health and law enforcement agencies are the best resource concerning applicable state laws.

133. Nowhere in the FDA's statement about what it is doing to protect public health does FDA state that it is presently seeking to ban the distribution, sale, purchase or consumption or to prevent consumer use. However, on its kratom website FDA states "While FDA continues to evaluate the available safety information about the effects of kratom, the agency encourages health care professionals and consumers to report any adverse reactions to the FDA's MedWatch program." Such statements fall far short of claiming that kratom is an illicit substance.

134. Instead, the FDA should comply with recommendations of Congress and follow the lead of more than a dozen states to accept kratom as a dietary ingredient and review new dietary

ingredient notifications submitted to the Agency by responsible industry participants, as well as other actions that would support public health and benefit consumers.

Opinion 12: The FDA has not attempted to ban marketing kratom or to suggest that marketing kratom is illegal or irresponsible through its warning letters to some companies that sell kratom. In fact, the FDA states that its approach in these warning letters is to protect public health and to guide acceptable marketing practices.

135. In some cases, the FDA may determine that a marketing claim crossed the line and could be interpreted as a drug claim, such as “works best as a sedative,” “for heroin and opiate withdrawal,” or “is great for pain relief and pain management.” If so, the FDA may send a warning letter that requests that the vendor correct the problem (e.g., remove and cease such claims) and inform the FDA of how the problem was corrected. Generally, as in the foregoing case, the vendor has a certain amount of time to correct the problem or at least explain to the FDA why it might take longer. A typical example of this is illustrated in the June 30, 2022, FDA letter to Omni Consumer Products.⁵

136. This is consistent with the FDA’s clarification of its position when asked to testify in the Southern District of California,⁶ as well as its 2024 update to its website noted earlier in this report. In that matter, the FDA declined to testify but took the position that it had not yet determined if kratom was hazardous.

137. Warning letters and product confiscation actions are not intended to ban kratom or prevent consumer access to kratom but rather to address specific issues that appear to warrant some remedial action.

138. The purpose of warning letters is rarely to remove categories of products from the market, but rather to stop and prevent inappropriate marketing practices. However, FDA could issue a series of warning letters for a specific ingredient based upon safety concerns rather than marketing claims. FDA has not issued this type of warning letter for products containing kratom to date.

139. In some cases, I understand that acting on the FDA’s import warning, mislabeled products have been seized by agents of the Department of Justice but later returned to the vendor for distribution to retailers (discussed in *United States v. Nine2Five, LLC*, Case No. 3:23-CR-00179-TWR (S.D. Cal.)).

140. This results in a marketing landscape with uncertain rules and regulations that can be easily misinterpreted by those who are unfamiliar with the FDA’s approach to kratom.

Opinion 13: For several years, the FDA has diverged from the DEA with respect to communications related to kratom science, safety and appropriate public health policy;

⁵ See FDA Warning Letter to Omni Consumer Products at <https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/omni-consumer-products-llc-dba-yokratom-634184-06302022>.

⁶ *United States v. Nine2Five, LLC*, No. 3:23-CR-00179-TWR (S.D. Cal.), ECF No. 110-8 at 2.

however, in the past few years, the FDA appears to have adopted approaches that are more consistent with the scientific evidence and in support of public health.

141. Three federal agencies—the DEA, FDA, and NIDA—monitor kratom use, safety and public health impact with their public attention increasing since about 2010. All three agencies have been involved in developing and interpreting kratom science, public health impact, and translation of such into public health policy and communications such as on their kratom specific websites.

142. NIDA is the U.S. and world leading funder of kratom research and the lead U.S. agency with responsibility for generating and assessing the science related to substances with central nervous system effect.

143. NIDA has contributed to FDA CSA drug scheduling recommendations since the 1970s. NIDA’s input was formally established as part of the protocol by which the Assistant Secretary of Health provides CSA scheduling recommendations to the DEA which is the agency with the designated authority to schedule drugs.⁷ After the 1985 Memorandum of Understanding, NIDA established the Biology of Dependence and Abuse Potential Assessment Section within the Clinical Pharmacology Branch of its Intramural Research Program (“Addiction Research Center”). I served as the first Section Chief, as well as Chief of the Clinical Pharmacology Branch, until I left NIDA in September, 1996.

144. The three agencies have not been closely aligned on whether kratom scheduling was in the interest of public health or the rational for scheduling kratom. Specifically, NIDA and later the DEA considered the importance of kratom as a path away from opioids and opioid overdose risks, as well as other health related effects of kratom that are reported by kratom users. The FDA initially took the position that people with opioid use disorder should use FDA approved drugs without recognizing that kratom was helping many people who found FDA approved drugs ineffective, not acceptable or not accessible (Grundmann et al. 2018; Henningfield et al. 2018a). NIDA has not voiced support for kratom prohibition by designating it as a Schedule I controlled substance. Neither has the DEA since October 2016, when it withdrew its August 2016 proposal to classify kratom (specifically mitragynine and 7-OH) as Schedule I drugs along with heroin and LSD.

145. The FDA has now moderated its position on kratom somewhat but has yet to announce an approach to provide regulatory safeguards without banning kratom, which would foreseeably lead to some “kratom users switching to highly lethal opioids” and other serious adverse consequences (Giroir, 2018).

146. In addition to differences across these three agencies, the public statements, regulatory approaches, and actual policy approaches of each of these agencies have evolved over

⁷ Memorandum of Understanding with the National Institute on Drug Abuse (Notice; 50 FR 9518-20; March 8, 1985), at https://archives.federalregister.gov/issue_slice/1985/3/8/9517-9520.pdf#page=2, accessed April 13, 2025.

the past one to two decades as kratom marketing, consumption, and reports in the general media and scientific literature have increased.

147. The differences across these three federal agencies and how their positions have evolved over time are relevant, as the following summaries of the actions of the three agencies show. Although the DEA, FDA and NIDA rely upon multiple lines of evidence, including surveillance data from other federal agencies such as the CDC, the Substance Abuse and Mental Health Services Administration, and the U.S. Poison Control Centers (PCC), the DEA, FDA and NIDA are more actively involved in kratom related public policy and product regulation.

148. The FDA also no longer provides any numerical estimates of kratom-caused deaths, which is a departure from the various estimates it provided in 2018, in which follow-up called into question the specific role of kratom in all of those deaths.

149. In most reports of kratom associated deaths, the contribution of kratom in the deaths is unclear at best. My current opinion with respect to kratom in general, and with respect to specific kratom death related assertions and complaints, is consistent with the report I developed for submission to the DEA in 2016 (Pinney Associates / Henningfield and Fant, 2016, p. 53-54):

150. A recently published, peer-reviewed article outlines well the position of the published studies:

“Although death has been attributed to kratom consumption, there is no solid evidence that kratom was the sole contributor to an individual’s death” (Warner et al., 2016). We do not rule out the possibility that there have been overdose deaths involving extremely high doses of kratom; however, to date, we have been unable to document a single death in which kratom overdose can reasonably be concluded to have been “causal” in the death. By any measure this is in stark contrast with what has been documented for most recognized drugs and substances of abuse. For example, CDC reported data for 2014, with limitations acknowledged, in which deaths were reasonably concluded to have been categorized substantially, if not exclusively, to an opioid (28,647 in 2014 or nearly 80 per day) or other drugs most notably including sedatives, alcohol, and stimulants (18,408 or about 50 per day) for a total of 47,055 or about 129 per day (Rudd et al., 2016).

As mentioned earlier, the very low risk of overdose poisoning and serious adverse events does not mean that they have not and will not occur. However, given the two decades during which consumption has increased to an estimated two or more million consumers in the US, in addition to far more extensive consumption in Southeast Asia, this is a substance and category of product with a remarkable safety record. It is not the profile of a serious or emerging public health problem that warrants drastic actions that would prohibit kratom consumers from continuing to lawfully purchase kratom. The safety record is all the more impressive given that kratom products have been marketed, prepared, and consumed without the level of regulatory oversight that is present for many other dietary supplements and natural products under the FDCA. Balanced and appropriate regulation seems vital to

maintain the safety record. This should be accompanied by increased surveillance to better guide kratom regulation going into the future.

151. The scientific evidence since 2016 continues to support this position, and the vast majority of the new science was generated by research supported by NIDA and published in peer-reviewed journals. It is also consistent with the approach adopted and communicated by the DEA and NIDA since 2016. The FDA was overruled due to its failure to consider the public health implications of a kratom ban and reliance on weak and misinterpreted evidence and data (*e.g.*, Giroir, 2018 and Giroir May 2021 tweet response to FDA Commissioner Scott Gottlieb who led FDA's statements and position on kratom in 2017 and 2018).

152. I agree with former Assistant Secretary for Health Dr. Giroir's evaluation of the Dr. Gottlieb-led 2017-2018 position that appears to be generally relied upon by some medical institutions (*e.g.*, Mayo Clinic).

153. Another example related to the DEA's approach was its inclusion of kratom on its list of Drugs of Concern as part of its broader concern about the introduction of synthetic psychoactive substances such as K2, Spice, and bath salts in 2008 (DEA, Drugs Forum 2008). The DEA later reported its detection of kratom (mitragynine specifically) in evaluating substances found in drug enforcement actions of illicit drug marketers and consumers in its mid-year 2015 Annual National Forensic Laboratory Information System (NFLIS) report which reported on mitragynine identifications (US DEA, 2015). Importantly, neither the DEA's Drugs of Concern listing nor its NFLIS detection reports included data or statements related to reasons for use or effects of use or harmfulness to consumers or public health (DEA, 2016). The DEA's action reflects its observation of increasing detection of kratom in some of its diverse efforts to detect and monitor potential emerging trends in the availability, distribution and use of substances that have psychoactive effects relevant to their use.

154. The DEA's statutory mission includes early detection of substances that might be of public health impact and the frequent designation of the substances as being on a "Watch List" and "Drugs of Concern," regardless of whether actual harm, abuse, or addiction have been documented.

155. I developed a summary of the DEA's initial kratom findings in an evaluation of kratom abuse potential according to the 8-factor analysis of the DEA and Controlled Substances Act. This evaluation was developed for submission to the DEA in response to its October 2016 requests for information related to kratom safety and abuse potential (Pinney Associates, led by Henningfield and Fant, 2016):

Mitragynine was first reported in the NFLIS system in 2010. From 2013 to 2015, mitragynine reports accounted for approximately 0.01% of total reports. Specifically, 181 mitragynine reports were recorded in 2013 (out of 1,540,647 total reports), 137 in 2014 (out of 1,511,313 total reports), and 129 in 2015 (out of 1,549,466 total reports). The fact that these identifications were a new category, albeit at very low rates, led the DEA to place mitragynine on its "watch list," meaning essentially that laboratories and investigators are encouraged to be alert for products potentially containing mitragynine and to be testing for mitragynine.

To provide some perspective of how mitragynine reports compare to opioids, Table 1 from the NFLIS July, 2015 special report on “Opiates and Related Drugs Reported in NFLIS, 2009-2014 (, July, 2015) is shown below (See Table 3). Among these substances, heroin accounted for 699,847 (48.64%), followed by oxycodone at 285,381 (19.83%), and hydrocodone at 235,417 (16.36%), together accounting for approximately 85% of the 1,438,933 reports. Mitragynine reports totaled 42 (0.03%) in the second six months of 2011 and 88 (0.06%) in the first six months of 2014, and totaled 458 (0.03% overall) through June, 2014.⁸

156. In 2018, I expanded and updated my 2016 8-factor analysis of the abuse potential of kratom in a peer-reviewed analysis and review of kratom abuse potential (Henningfield, Fant & Wang, 2016) as follows:

In 2016, the DEA published its notice of intent to temporarily place mitragynine (MG) and 7-hydroxymitragynine (7-OH-MG) (the primary active alkaloids of kratom) into Schedule I of the Controlled Substances Act (CSA) (US Drug Enforcement Administration 2016a; Ingraham 2016). Within weeks, DEA received thousands of comments from the public, a bipartisan response from the US Congress, and legal-regulatory arguments from the AKA by its representatives Hogan Lovells (American Kratom Association and Botanical Education Alliance 2016; Hogan Lovells 2016; Wing 2016). Comments highlighted personal experiences and use in order to abstain from previous dependencies on opioids and to treat a variety of maladies including pain and depression with few risks of side effects and serious adverse events. In response, the DEA announced less than 2 months after its initial emergency action that it was withdrawing its proposed intent to schedule kratom and would be seeking input from the Food and Drug Administration (FDA), the National Institute on Drug Abuse (NIDA), as well as comments from the public, in order to develop a full abuse potential assessment according to the eight factors of the CSA and develop regulatory recommendations (US Drug Enforcement Administration 2016b; Gruley 2016).

157. In withdrawing its proposal to schedule kratom, the DEA included the following rationale in its October 6, 2016, Federal Register Announcement (DEA, <https://www.federalregister.gov/documents/2016/10/13/2016-24659/withdrawal-of-notice-of-intent-to-temporarily-place-mitragynine-and-7-hydroxymitragynine-into>):

On August 31, 2016, the Drug Enforcement Administration (DEA) published in a notice of intent to temporarily place mitragynine and 7-hydroxymitragynine, which are the main psychoactive constituents of the plant *Mitragyna speciosa*, also referred to as kratom, into schedule I pursuant to the temporary scheduling provisions of the Controlled Substances Act. Since publishing that notice, DEA has received numerous comments from members of the public challenging the scheduling action and requesting that the agency consider those comments and accompanying information before taking further action. In

⁸ The 2015 DEA NFLIS Special Report on which the above statements are based is listed in the references (U. S. DEA, 2015).

addition, DEA will receive from the Food and Drug Administration (FDA) a scientific and medical evaluation and scheduling recommendation for these substances, which DEA previously requested.

DEA is therefore taking the following actions: DEA is withdrawing the August 31, 2016 notice of intent; and soliciting comments from the public regarding the scheduling of mitragynine and 7-hydroxymitragynine under the Controlled Substances Act.

158. Since the DEA's 2016 withdrawal of its August 2016 kratom scheduling proposal, it has not reported kratom detection data in its annual NFLIS reports, and it has never included kratom or its alkaloids in its annual National Drug Threat Assessment (NDTA) reports. However, it continues to monitor kratom, consistent with its mission to protect public health by surveillance and monitoring.

159. In sum, the FDA's formal kratom scheduling recommendation was transmitted to the DEA by the protocol required by the Controlled Substances Act to permanently schedule kratom as a Schedule I drug by the Assistant Secretary for Health, Dr. Giroir (Giroir, 2018). In response to concerns by leading kratom researchers and evidence from surveys, the Department of Health and Human Services conducted its own review of the evidence for scheduling and its potential public health implications and rescinded the FDA's recommendation.

160. The most recent example of the FDA's evolving opinion related to kratom safety is its focus on the mitragynine metabolite, 7-OH. The level I and others recommended as unlikely to cause harm was adopted by the American Kratom Association's Good Manufacturing Standards Program, now in its 4th revised version (American Kratom Association, 2024). Related to 7-OH, it includes the following requirement (that the OPMS product at issue meets):

A declaration that any level of 7-hydroxymitragynine does not exceed the alkaloid fraction that is greater than two percent (2%) of the overall alkaloid composition of the product.

Any product that contains a level of 7-hydroxymitragynine greater than this two percent (2%) limit cannot be marketed, labeled, or contain any reference on its packaging that it is a kratom product.

161. On July 29, 2025, the FDA issued a warning specific to 7-OH, distinguishing this chemical, from "kratom" in a manner that is consistent with my opinions in three documents: (1) its own review of 7-OH pharmacology, toxicology and safety (FDA, 2025d), (2) its approach to preventing a new potential wave in the opioid epidemic, given the categorization of 7-OH as a "potent opioid" (FDA, 2025b), and (3) a "Dear Colleague" warning letter to health professionals (FDA, 2025c). In these materials, FDA was careful to make clear that its actions pertain to 7-OH products, which "no longer represent botanical kratom" (FDA, 2025d, p. 5).

162. For example, in the "Dear Colleagues" warning letter for public health professionals released on July 29, 2025, FDA Commissioner Martin A. Makary included the following statement that is consistent with other statements made and materials released at FDA's press conference and on its website:

I am writing to warn you about an opioid that few physicians may be aware of. It's called 7-hydroxymitragynine (7-OH).

7-OH is found in trace amounts in the kratom plant leaf. But this is not our focus. Our primary concern is the concentrated form of 7-OH. This is an important distinction. These concentrated 7-OH opioid products are far more dangerous than traditional kratom leaf products.

Concentrated 7-OH products have exploded in popularity in recent years, with vape shops, gas stations and corner stores selling pills, gummies, candies, and even eye-catching products like ice cream cones containing 7-OH. You may also see 7-OH referred to as 7-OHMG, 7-Hydroxy, 7-HMG, or 7. Additionally, some kratom leaf products marketed as "spiked" or "enhanced" may contain 7-OH at a level 500% higher than would be naturally expected in kratom leaf.

(FDA, 2025c).

163. In sum, as of July 29, 2025 (FDA, 2025a, b, c, d), FDA has made it clear that its concern is not kratom, nor the low amounts of 7-OH that may occur naturally in kratom leaves and in many products. However, it expressed serious concern about products with highly concentrated levels of 7-OH. The OPMS products at issue, as discussed earlier, do not contain such high levels of 7-OH.

Rebuttal

Joseph Thundiyl, M.D., opinions

Thundiyl offers two opinions relevant to plaintiffs claim that kratom caused Harmony Moller's death. These are the first two (a and b) of his four opinions

a. I agree with the Medical Examiner Report of Forensic Pathologist, Michael DeFatta, M.D. insofar as mitragynine use contributed to and caused Harmony Moller's death.

b. I agree with the opinions of Christopher Williams, Ph.D. submitted herewith regarding the pharmacology and risk profile of kratom. I agree with the opinions of Ron Wharton, M.D. submitted herewith, specifically, that Harmony Moller's death was an adverse cardiorespiratory event caused by kratom."

It is not clear what evidence supports his opinions as there is no discussion in his report. Moreover, although he states that he agrees with the opinions of Michael DeFatta, Christopher Williams and Ron Warton, all of them came to conclusions that are not supported by the evidence as I note below in my comments on their opinions.

Furthermore, the reliance materials that he cites include published reviews and studies that do not support his opinions or those of DeFatta, Williams, and Warton (e.g., Henningfield et al. 2018, 2019, 2021, 2022; Hill et al. 2022; Papsun 2019; Wilson et al. 2020; McCurdy, 2021; Swogger et al. 2022; World Health Organization, 2021). The foregoing is not comprehensive, however given the very limited of evidence that kratom consumption in the absence of other substances is a cause of death by any known pathophysiological mechanism, and nor the cardiovascular abnormalities described in the coroner's report which stated (without evidence of causality) that the "CAUSE(S) OF DEATH: [was] Abnormally high left coronary ostia takeoff exacerbated by mitragynine use." (Coroner's Report Pursuant to R.S. 44:19 (E)(3), Christopher Tape, March 11, 2025).

It is simply not clear on what actual evidence Thundiyl's opinions are based.

Christopher Williams, PhD, opinions

On the first page of his report, Williams states as follows

"My goal in this case is not to identify cause of death, nor is it to provide clinical diagnostic information. Rather, my role is to provide the scientific background on the pharmacological activity of Kratom (*mitragyna speciosa*) alkaloids, and the mechanistic underpinnings of its drug-like effects when consumed or utilized as a so-called nutritional supplement or food. My opinions herein are given to a reasonable degree of scientific certainty."

Williams' main case-specific opinion on the second page of his report is as follows:

“The cause of death was officially documented as “abnormally high left coronary ostia takeoff exacerbated by mitragynine use”. It is my opinion that the mechanisms of Kratom alkaloid activity support this conclusion, and I agree with the findings of Dr. Thundiyl and Dr. Wharton in this regard.”

I note that Williams and Thundiyl both note that they agree with the other, with neither of them actually providing an evidence supported basis for their opinions. Moreover, both Williams and Thundiyl included reliance materials that do not support their opinions.

Williams’ “scientific background” includes only seven citations, two from 2004 and 2014 which do not support the conclusion that kratom was the cause of the cardiovascular abnormality reported by the coroner – specifically the “Abnormally high left coronary ostia takeoff exacerbated by mitragynine use.” (Coroner’s Report Pursuant to R.S. 44:19 (E)(3), Christopher Tape, March 11, 2025).

Nor do the other five citations support Williams’ stated opinion. In fact, one of these seven citations was for the sole major clinical trial, conducted by a major independent contract research organization, with Health Canada regulatory input, and commissioned by Johnson Foods, determined that a range of kratom doses and types did not produce serious cardiovascular events or side effects (Huestis et al. 2024). This study was cited by Williams but not its findings which do not support Williams’ opinion related to kratom’s contribution to Harmony Moller’s death. Note that I contributed to the design of the Huestis et al. study but did not co-author the publication.

The “scientific background” is limited in scope and depth in approximately two pages of text. It includes statements that are not supported by recent, reliable and replicated studies but rather apparently “stands to reason” by Williams.

For example, on page 3 Williams states as follows:

“With largely similar pharmacological mechanisms of action and *similar potency to prescription opioids* [italics in original], it stands to reason that kratom alkaloids will mirror those of opioids. Among the most significant opioid-related adverse effects is respiratory depression.”

He did not discuss the increasingly documented extensive differences between kratom alkaloids that have actually been compared to morphine that find differences in classic opioids measures including rewarding effects, in animals, withdrawal, respiratory effects, behavioral generalization in drug discrimination studies.

The exception is 7-OH or 7HMG which can produce similar effects as morphine when injected intravenously and in animal self-administration studies as recently reviewed by FDA (Reissig et al. 2025; Henningfield, et al. 2024, 2025). But the products claimed by plaintiff to be used by Harmony Moller only contained very low levels of 7HMG that have not been demonstrated to be harmful. Furthermore, respiratory depression has not been documented in animal studies in which mitragynine was administered at very high levels and did produce high blood concentrations of

7HMG (e.g., Gonzalez et al. 2025; Henningfield et al., 2022 [respiratory study], 2024; Hill et al. 2022 [respiratory mouse study]; Kruegel et al. 2019).

Williams' scientific background and conclusion that kratom mirrors the effects of opioids is at odds with the understanding the neither kratom in general nor products such as purportedly used by Harmony Moller "mirror" the effects of opioids, have "largely similar mechanisms of action" and/or "similar potency to prescription opioids."

However, as I discussed in this report, intravenous administration of high doses of 7-OH has been demonstrated to produce opioid-like reward and respiratory depression in rodent models.

As discussed in my report, kratom and mitragynine differ from opioids across a broad range of measures of mechanism of action, opioid-like brain rewarding effects, respiratory depression, overdose deaths, or real-world patterns of use and associated physical dependence and withdrawal as have been observed for morphine, heroin, oxycodone and fentanyl type opioids. If Williams' statement was accurate, then kratom and mitragynine would likely be scheduled in the Controlled Substances Act as discussed in my report and elsewhere (Henningfield et al. 2022 [8FA], 2024, 2025a [Introduction to Kratom book], b [8-Factor Analysis]; Reissig et al. 2025; WHO, Expert Committee on Drug Dependence, 2021).

Williams' science summary simply does not reflect the increasingly documented extensive differences between kratom alkaloids that have actually been compared to morphine that find differences in classic opioids measures including rewarding effects, in animals, withdrawal, respiratory effects, behavioral generalization in drug discrimination studies. The exception is 7HMG which can produce similar effects as morphine when injected intravenously and in animal self-administration studies as recently reviewed by FDA (Reissig et al. 2025; Henningfield, et al. 2024, 2025).

Williams' very brief overview of the "scientific background on the pharmacology of kratom" includes misunderstandings of both mitragynine and 7-hydroxymitragynine (7-OH). Some of his statements are generally consistent with observations made a decade or more ago, even by FDA, but are no longer accurate and do not overall reflect the current state of kratom science, which thanks substantially to research support by the NIDA, has been numbering more than 100 publications per year for the past few years and appears to be accelerating still as I discussed earlier in my report.

For example, 7HMG, is now known to be not a kratom constituent but a metabolite and its gradual emergence in the blood following oral consumption apparently contributes to its low risk of association with respiratory depression and other adverse effects. Such effects may require intravenous administration of large doses or possibly oral consumption of large doses of highly concentrated 7-OH, neither of which are known to be relevant to Harmony Moller (Gonzalez et al. 2025; Henningfield et al. 2024; Hill et al. 2019; Kruegel et al. 2019; Reissig et al. 2025).

Furthermore, Williams' summary of kratom pharmacology cannot be considered a scientifically sound and evidence-based foundation for his opinions and those other plaintiff's experts who may rely on his summary and opinions (as expressed by Thundiyil).

Williams also relies on the FDA Adverse Event Reporting System (FAERS) database to support his statement that “MG was associated with a greater incidence of ventricular arrhythmia/cardiac arrest than any other drug tested, including methadone. *In 39% of those cases, MG exposure was indicated in the absence of concurrent QTc prolonging drugs*, thereby suggesting that MG was the primary driver of cardiotoxicity” [italics in Williams original].

Williams apparently does not understand what FDA itself states about the limitations of FAERS for assessing causality. Reports to FAERS are spontaneous reports from manufacturers, healthcare professionals, and the public. The reports within FAERS are heterogeneous, varying widely in how events are described and in their completeness and reliability. In many cases, it is unclear whether the reported product caused the event, whether other products were used, or whether pre-existing conditions may have caused or contributed to the event. FDA explicitly cautions that FAERS data alone cannot be used to establish causality. (Reference: <https://www.fda.gov/drugs/fdas-adverse-event-reporting-system-faers/fda-adverse-event-reporting-system-faers-public-dashboard>)

For example, in a recent report by FDA staff addressing 7HMG (7-OH) FDA itself stated as follows in its summary two cases:

“Although FDA’s Adverse Event Reporting System (FAERS) has documented cases reporting adverse events (13 cases, including 2 deaths) suspected to involve 7-OH, ambiguity about the contributory role of 7-OH from uncharacterized products or concomitant medications and underlying disease limits interpretation” (Reissig et al., 2025).

Note that this same report led by Reissig made clear that FDA’s kratom related serious safety concerns were specific 7-OH.

Related to the general safety and risks of 7-OH, it is important to note that as I discussed in the eight factor analysis of 7-OH that I led and submitted to DEA, FDA and NIDA, I agree with FDA’s characterization of 7-OH. This includes the conclusion that at least in the intravenous form and plausibly, highly concentrated marketed 7-OH products (not the focus of this litigation) have opioid like effects.

However, in contrast to the tens of thousands of opioid attributed overdose deaths annually in the US, FDA was only able to document two potential 7-OH deaths two date.

Thus, whether MG itself contributed to the events reported in the FAERS database cannot be ascertained from the reports.

Williams seems to have dismissed the potential contribution of diphenhydramine, promethazine and delta-9 THC, that is obtained by the use of cannabinoids which have well known cardiovascular effects (See NIDA at <https://nida.nih.gov/research-topics/cannabis-marijuana#long-term-health-cannabis> of cannabis use and Paulraj S, Upreti P, Tamirisa K,

Batnyam U. Arrhythmias and cannabis use: A comprehensive overview. *Heart Rhythm* 02. 2024;6(1):78-85. Published 2024 Nov 6. doi:10.1016/j.hroo.2024.10.020)

Williams states (on page 4) as follows: “Of note, the levels of the diphenhydramine (64 ng/ml) and promethazine (18ng/ml) are in accordance with expected levels in therapeutic drug usage, suggesting that these drugs alone were not used at a level that should precipitate cardiorespiratory toxicity (toxicity is apparent near (100ng/ml range for either drug). Additionally, the typically benign elevated heart rate that is associated with cannabis use might present another potential unrecognized interaction with Kratom alkaloids.”

I note that the actual level of intake of cannabinoids by Harmony Moller cannot be ascertained by postmortem blood sampling and analysis because delta-9 THC levels decline very rapidly.

Williams did not similarly comment on plasma mitragynine levels which were low and well within the range that has been observed in participants in NIDA support research (discussed in Henningfield et al. 2024), and FDA safety study (Reissig et al. 2024); and a full scale clinical safety study conducted by a major contract research Organization (Huestis et al. 2024a,b).

For example, Dr. Marilyn Huestis presented data at the American Academy of Forensic Sciences (AAFS) Annual Meeting in February 2024 showing that there were dose-proportional increases of mitragynine Cmax after single doses of Mitra-Leaf ($\approx 17, 32, 57$, and 125 ng/mL at $6.65\text{--}53.2$ mg), and reached slightly higher values at steady state with multiple dosing ($\approx 21, 34, 75$, and 143 ng/mL across the same dose levels).

She concluded that, in contrast to mitragynine, blood levels of 7-hydroxymitragynine remained much lower, with single-dose Cmax values of about $3\text{--}23$ ng/mL and steady-state Cmax values of about $3\text{--}22$ ng/mL, showing no meaningful accumulation. Overall, these data demonstrate predictable, linear increases in mitragynine exposure, minimal changes in 7-OH-MG with repeated dosing, and a consistently low 7-OH-MG to mitragynine ratio at all doses.

Mitra-Leaf was found to be generally well tolerated by participants at all dose levels and there were no reported serious cardiovascular adverse events or other serious adverse effects.

Part of the problem with basing opinions on population level reports of reported cardiovascular events associated with kratom and most case reports to date, is that they typically have little information on dosing levels, the nature of the kratom product, other substances that were used and the potential other health conditions. Papsun et al. (2023) report rarely seeing death at levels below 1000 ng/mL, a figure that should not be interpreted as the determination that 1000 ng/mL is a threshold for risk but it is consistent with the evidence it is likely that levels of several hundred ng/mL are achieved by many of the millions of kratom consumers in the US and yet few deaths per year in which there was no evidence of other drug use. As I discuss in this report, that is part of the reason that FDA no longer provides numerical estimates of kratom associated deaths, but rather agrees with NIDA that kratom alone deaths are rare and generally associated with other drugs (See also Giroir, 2018 in my report).

Harmony Moller did show evidence of at least four different substances, with none of them at apparently high levels of exposure, except possibly cannabis in which it cannot be concluded as to what her level was at the time of her death. It could have been very high if she had consumed cannabis in the hours before her death.

Thus, I am in general agreement with the first clause of Williams' following summary concluding sentence on page 4: "[C]ausality is difficult to ascertain in cases of polypharmacy induced drug effect." That is, I agree that causality is difficult to ascertain in cases of polypharmacy. Moreover, as I discussed earlier in my report, both FDA and NIDA agree that kratom associated deaths are "rare" and generally involve other substances.

Regarding the second clause of his sentence: "the mechanistic underpinnings are present for significant drug-drug interactions involving MG and 7HMG," he provides no evidence-based foundation, though the clause was vague and did not address whether he was attempting to provide a foundation for cardiovascular effects, respiratory depression or any other effects. Nor did he cite any drug-drug interactions studies involving "MG and 7HMG" or other kratom alkaloids. Perhaps this is because there have not been systematic drug-drug interactions studies involving these alkaloids related to cardiovascular, respiratory or central nervous system effects, with the exception of some studies assessing the effect of naloxone on some mitragynine, 7-OH effects (e.g., Henningfield et al. 2024, Reissig et al. 2025)

Ronald H. Wharton MD, FACC, FASE

I will address Dr. Wharton's third opinion which is as follows on page 3 of his report: "In my opinion, more likely than not, Harmony Moller died from a cardiorespiratory adverse event induced by consumption of kratom."

He supports this with the following observation: "There are multiple reports in the medical literature that associate the use of kratom products with the development of ventricular tachycardia and ventricular fibrillation (VT/VF), which cause the heart to stop beating."

It is not clear why he did not raise cannabis as a potential contributor since cannabis has been far more extensively documented to produce ventricular fibrillation than is the case for kratom. (See my discussion above addressing Williams and including NIDA cannabis website and Paulraj S, Upreti P, Tamirisa K, Batnyam U. Arrhythmias and cannabis use: A comprehensive overview. Heart Rhythm O2. 2024;6(1):78-85. Published 2024 Nov 6. doi:10.1016/j.hroo.2024.10.020)

The conclusion that kratom was the primary cause of death, or even contributing cause, in Harmony Moller cannot be inferred from plasma mitragynine levels, as no known level has been identified as a lethal dose by kratom use alone or in combination with opioids, stimulants, sedatives or other drugs. Having said this, I and many experts urge caution in the use of kratom with other drugs, because although no particular combination of kratom/mitragynine with other drugs has emerged as a consistent cause of death in the more than 80,000 annual drug overdose deaths in the United States, and no animal interaction studies, it seems prudent to urge caution in general conclusions.

How Wharton came to the conclusion that it is “more likely than not, Harmony Moller died from a cardiorespiratory adverse event induced by consumption of kratom” is not evident to me in his report.

Evelyn Cadman, BS, CN

I will briefly comment on two aspects of Cadman’s opinions, her disagreement that kratom can be represented as a “food” and comments that warnings on the products in dispute were not adequate.

Page 20 of Cadman’s report states “Kratom is Not a Food.” I agree that kratom is not a conventional food necessary for health and wellbeing, however it is regulated in a special category of foods by FDA’s Office of Dietary Supplements which is in the Human Foods Program of FDA’s Center for Food Safety and Applied Nutrition (CFSAN). Key definitions and concepts for dietary ingredients and dietary supplements merged with the 1994 Dietary Supplement and Health Education Act (DSHEA) of 1994.

As I state above in Paragraph 112, “its regulatory place as a dietary ingredient as defined in the United States Code, Title 21-FOOD AND DRUGS, Chapter 9 Federal Food Drug and Cosmetic Act Subchapter Definitions (U.S.C § 321).”

I quote a former director of FDA’s Office of Dietary Supplements from a recently published review article in a book that I co-edited. It is as follows:

DSHEA provided a definition of what a dietary supplement is, which can be found in section 201(ff) of the FDCA.⁹ Among other attributes, the definition of a *dietary supplement* requires that it contain at least one dietary ingredient, be swallowed into the alimentary canal, not mimic or be intended to take the place of a conventional food, and not contain a dietary ingredient that was approved as a drug or studied, under an Investigational New Drug authorization, as a drug prior to being marketed as a dietary ingredient.¹⁰

The definition of a dietary supplement includes that of a *dietary ingredient*, defined as: (1) a vitamin, (B) a mineral, (C) an herb or other botanical, (D) an amino acid, (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake, or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in (A) through (E).¹¹

Thus kratom, as a botanical, and its extracts and constituents (e.g., alkaloids, flavonoids, metabolites), qualify as dietary ingredients for use in dietary

⁹ 21 U.S.C. § 321(ff).

¹⁰ 21 U.S.C. § 321(ff)(3).

¹¹ 21 U.S.C. § 321(ff)(1).

supplements. (Durkin, Grundmann, and Smith, *Kratom*, Regulation and policy regarding kratom-derived dietary supplements and direct-to-consumer sales, 2026).

As I discussed in my report, I have worked with FDA before and during the passage and implementation of DSHEA and more extensively on dietary regulation over the past decade. I agree with Durkin et al. summary.

Regarding warnings

On page 12 Cadman cites Papsun et al. 2023 to support her conclusions about warnings. She states, “The warning on the OPMS kratom package... adverse effects and death.” She seems not to understand that detailed product warnings typically emerge as a collaborative process by FDA and product sponsors to determine what risks have actually been determined to be posed by that consumption of a specific product and not simply events that have sometimes been associated with consumption often along with other products and may be better described as undetermined, polypharmacy or at extremely high dosage levels

In fact, as I discussed in my report and have earlier testified, developing warnings for dietary products as for drugs is not an exercise of simply warning people of anything that has been reported. Such reports are only the starting point for a process that must involve FDA. I have called for FDA to develop product standards and appropriate warnings for more than a decade, as have kratom product sponsors including those who have submitted NDINs’ FDA has yet to act.

Sarah D. Kowitt, PhD

Dr. Kowitt’s primary opinion is stated on page 2 of her report as follows: “It is my opinion that the warnings on the kratom packages discovered near Ms. Moller were not adequate for the reasons outlined below.”

Dr. Kowitt’s report is a summary of research, largely academic and public health on examples of warnings, warning effectiveness, and warning research, primarily addressing tobacco products. Notably absent is discussion of the FDA process by which warnings are developed and how sponsors work with FDA on that process. The only reference to FDA is with respect to FDA’s website which provides a list of potential concerns and warnings but not an evidence-based list that would necessarily emerge from an FDA effort to development warnings for kratom.

Dr. Kowitt does provide, on page 6, an example of an FDA required warning on iron-containing dietary supplements. I was not involved in the generation of that warning, but this illustrates the result of an FDA warning generating process that results in concise, evidence-based statements.

I have worked with FDA staff on warnings for drugs (both prescription and over-the-counter consumer products), and tobacco for several decades. It is an elaborate process that takes into consideration some of the concepts discussed by Dr. Kowitt.

It is not a matter of listing adverse effects that have been associated with a product. As an example, kratom use has occasionally been associated with liver abnormalities. Whether serious liver abnormalities were contributed to by kratom consumption or by the decades of consumption often at high levels of acetaminophen, alcohol and other substances which are known to carry very high risks of liver abnormalities, disease and death, especially in people with pain and addictions who are among the prominent reason for kratom use by millions of people, or kratom or both is not at all clear. FDA could help sort that out and determine what warnings are appropriate and how they should be worded.

Dated: December 18, 2025

/s/ Jack E. Henningfield
Jack E. Henningfield, Ph.D.