AMERICAN KRATOM ASSOCIATION

September 24, 2018

Dr. Brett Giroir
Assistant Secretary (Office of the Assistant Secretary for Health)
Department of Health and Human Services
Hubert H. Humphrey Building, Room 716G
200 Independence Avenue, SW
Washington, DC 20201

Sent VIA Email and Certified Mail

Dr. Giroir:

On behalf of the nearly 5 million Americans who safely consume the natural botanical kratom, we respectfully request you recall the kratom scheduling recommendation that was sent by your office to the Drug Enforcement Administration (DEA) in November 2017, and direct the U.S. Food and Drug Administration (FDA) to conduct a comprehensive re-evaluation of its data on kratom to conform with existing and emerging science with regard to its addiction and safety profile. Additionally, based on the conclusions of a recent review of alleged overdose deaths the FDA had claimed were "associated" with kratom use conducted by the National Institutes on Drug Abuse (NIDA), we ask that you direct the FDA to commence appropriate regulatory actions to remove adulterated and contaminated products from the market that are responsible for the deaths the FDA has previously associated with the use of kratom.

As you are aware, on November 14, 2017 the FDA issued a public health advisory on risks associated with the use of kratom[1] and then FDA Commissioner Scott Gottlieb made public statements that the FDA had completed the required 8-Factor Analysis supporting its recommendation to the DEA for kratom to be listed as a Schedule I substance. Pursuant to provisions of the Controlled Substances Act (CSA), the Secretary of Health and Human Services (HHS) has delegated to the Assistant Secretary of Health (ASH) the authority to make domestic drug scheduling recommendations.

[1] Statement from FDA Commissioner Scott Gottlieb, M.D. on FDA advisory about deadly risks associated with kratom, November 14, 2017.

In addition, a Memorandum of Understanding between NIDA and the FDA was published in the Federal Register[2] and recognizes FDA's commitment to collaborate fully with NIDA in the development of such recommendations because of NIDA's expertise in investigating and evaluating the potential for abuse associated with drug products.

The FDA's conclusions on the safety and abuse potential of kratom have faced significant challenges from a group of widely-recognized scientists who strongly disagree with the FDA, and argued persuasively in a letter to Congressional Leaders that, "[B]ased on the substantial science and safety signal data, we conclude that kratom does not meet the statutorily mandated criteria for Schedule I substances based on their potential for abuse, safety, dependence liability, and medical use (if any).[3]" These scientists also wrote to the White House and the DEA on February 8, 2018 and addressed the unintended consequence of the scheduling of kratom:

> "It is our collective judgment that placing kratom into Schedule I will potentially increase the number of deaths of Americans caused by opioids because many people who have found kratom to be their lifeline away from strong opioids will be vulnerable to resumption of that opioid use, whether their prior opioid use was for relief of pain or due to opioid addiction. This opinion is supported by four national surveys conducted in the past two years, as well as decades of studies in the US and in Southeast Asia, where kratom has been used as a safer alternative to opioids for more than a century. Failure to evaluate this potential outcome of any proposed scheduling of kratom would directly contradict the expressed purpose of the enactment of the CSA by the U.S. Congress, to protect the safety of consumers. Perversely, it is foreseeable that such an action may lead to the deaths of people and worsen the opioid crisis, not mitigate it.[4]"

There are two central questions that are the pillars of the FDA's scheduling recommendation: (1) the safety profile of kratom's alkaloids and whether a kratom user can overdose and die from kratom use; and (2) whether the kratom alkaloids are dangerously addictive. The FDA has

[2] Federal Register/Vol. 50. No. 46/Friday, March 8, 1985, FDA-225-85-8251, Memorandum of Understanding with the National Institute on Drug Abuse, page 9518 – 9520.

[3] Scientist letter to Congressional Leadership, Senate Majority Leader Mitch McConnell, Senate Minority Leader Charles Schumer, House Speaker Paul Ryan, House Minority Leader Nancy Pelosi, June 21, 2018, copy attached.

[4] Scientist letter to Kellyanne Conway, Counselor to the President, The White House, and Robert W. Patterson, Acting Administrator, Drug Enforcement Administration, February 8, 1018, copy attached.

relied upon various reports of 44 kratom associated deaths that it referenced both in its November 14, 2017 issuance of a public health advisory, and on February 6, 2018 where FDA cited additional adverse events associated with kratom use.

The AKA has aggressively petitioned the FDA and NIDA to re-evaluate the supporting data on these claims related to kratom associated deaths, and on July 2, 2018 NIDA posted a change to its DrugFacts web page to include a new section header:

> "*Can a person overdose on kratom?*
>
> *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."*

This statement directly contradicts the FDA claims on deaths associated with kratom, and after AKA expressed support for that conclusion, it was quickly removed, and NIDA announced it was commencing a collaborative review of the adverse event data with the FDA.

On Thursday, September 20, 2018, nearly two months after the review was commenced, NIDA posted the following update on its DrugFacts web page:

> "*Can a person overdose on kratom?*
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> *In 2017, the Food and Drug Administration (FDA) began issuing a series of warnings about kratom and now identifies at least 44 deaths related to its use, with at least one case being investigated as possible use of pure kratom. Most kratom associated deaths appear* ***to have resulted from adulterated products (other drugs mixed in with the kratom) or taking kratom along with other potent substances, including illicit drugs, opioids, benzodiazepines, alcohol, gabapentin, and over-the-counter medications, such as cough syrup****. Also, there have been some reports of kratom packages as dietary supplements or dietary ingredients that were* ***laced with other compounds that caused deaths****.[5]" (****emphasis added****)*

NIDA cites the FDA claim that at least one case is being investigated as possible use of pure kratom. The FDA made that statement on its investigation into a pure kratom death on

[5] https://www.drugabuse.gov/publications/drugfacts/kratom

February 6, 2018[6], and now more than 7 months later there is not any corroborating evidence produced by the FDA to validate that claim.

The AKA has consistently maintained that the disinformation circulated by the FDA is based on the fact that these kratom deaths are associated with deliberate adulteration of kratom products, polydrug use, or underlying health conditions of the decedent. The NIDA conclusion agrees with AKA's position, and more importantly removes one of the two pillars the FDA has used to justify its recommendation for kratom to be banned as a Schedule I substance under the CSA.

The second pillar of the FDA scheduling recommendation is whether the kratom alkaloids are dangerously addictive under standards required for scheduling under the CSA. There have been numerous scientific studies that called the FDA's conclusions into question on the kratom addiction issue, but a definitive study published in Addiction Biology on June 27, 2018[7] is the first to use an animal study to investigate how kratom's two main alkaloids, mitragynine and 7-hydroxymitragyine, affects the brain. Their research shows that mitragynine, present at moderate levels in the plant, has no potential for addiction and reduces opiate consumption. On the other hand, they showed that 7-hydroxymitragynine (7-HMG), present at very low levels in the plant, has high abuse potential and may increase consumption of other opiates.

Jack Henningfield, Ph.D., at Pinney Associates, and one of the world's experts on addiction and safety profiles of substances, provided the rationale for why this study is so significant:

> "This is an important study that addresses the addictiveness of kratom," says Jack E. Henningfield, Ph.D., at Pinney Associates, a health consulting firm. "It shows that the major naturally occurring constituent responsible for the health-related effects of kratom, mitragynine, is of very low abuse potential. A second substance, 7-HMG, which naturally occurs at such low levels in kratom that it might be of minimal health consequence, has higher abuse potential. This has at

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[6] Statement from FDA Commissioner Scott Gottlieb, M.D., on the agency's scientific evidence on the presence of opioid compounds in kratom, underscoring its potential for abuse, February 6, 2018, "Overall, many of the cases received could not be fully assessed because of limited information provided; however, one new report of death was of particular concern. This individual had no known historical or toxicologic evidence of opioid use, except for kratom. We're continuing to investigate this report . . ."

[7] Addiction Biology, *Abuse liability and therapeutic potential of the Mitragyna speciosa (kratom) alkaloids mitragynine and 7-hydroxymitragynine,* Scott E. Hemby, Scot McIntosh, Francisco Leon, Stephen J. Cutler, Christopher R. McCurdy, June 27, 2018, https://doi.org/10.1111/adb.12639

> least two regulatory implications. First, the findings do not support the FDA's claim that kratom is a narcotic-like opioid. Second, in regulating kratom products, the FDA could set standards to ensure that no kratom product contain levels of 7-HMG exceeding those that are commonly present in kratom leaves and products.[8]"

The only way that 7-HMG can present a public health threat is if it is artificially refined, purified, or concentrated, and any kratom product that is marketed with artificially elevated 7-HMG levels is either an adulterated product or subject to a new dietary ingredient (NDI) application to the FDA under provisions of the Dietary Supplement Health and Education Act of 1994 (DSHEA).

The critical point is that there is no scientific basis for the FDA to claim that the natural botanical plant kratom is dangerously addictive, and thus removing the second pillar of the FDA scheduling recommendation. Dr. Hemby observed that MG was not addictive "at all – in fact, it appeared to have the opposite effect.[9]"

Congress never intended for the Controlled Substances Act (CSA) to be used to ban substances that were deliberately adulterated with other toxic or deadly drugs that cause deaths, and nothing in the statute or the legislative history permits this abuse of discretion in the scheduling recommendation initiated by the FDA. There is not a single instance in the history of DEA scheduling where a substance was banned because it had been deliberately adulterated with a separate deadly drug.

The FDA appears to be deliberately violating the provisions of the Information Quality Act[10] by widely disseminating incomplete, inaccurate, biased, and unreproducible information to local medical examiners and coroners incorrectly blaming kratom for deaths that were actually caused by polydrug use or deliberately adulterated kratom products. In extrapolating the data to a faulty conclusion—in an effort to place kratom as a Schedule I substance under the CSA — the FDA's logic would require the prohibition of caffeinated

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[8] High Point University, *Professor's Research Shows Therapeutic Potential for Kratom,* June 29, 2018, http://www.highpoint.edu/blog/2018/06/professors-research-shows-therapeutic-potential-for-kratom/

[9] Business Insider, *A mysterious supplement has a viral following of people who take it for addiction — and researchers say it's too compelling to ignore,* Erin Brodwin, July 2, 2018.

[10] Section 515 of the Treasury and General Government Appropriations Act for Fiscal Year 2001, frequently referred to as the "Information Quality Act," 44 U.S.C. 3516, note ("IQA"), 3Pub. L. 106–554, § 1(a)(3) [title V, § 515], Dec. 21, 2000, 114 Stat. 2763, 2763A–153.

products, including even Coca-Cola and coffee, because someone deliberately laced those products with "potent substances, including illicit drugs, opioids, benzodiazepines, alcohol, gabapentin, and over-the-counter medications, such as cough syrup." In fact, it could be applied to anything, even broccoli, once it has been contaminated with a dangerous substance.

We respectfully request the immediate recall of the HHS scheduling recommendation on kratom from the DEA and ask the 8-Factor Analysis to be returned to the FDA for a comprehensive re-evaluation of the science required to support any such scheduling recommendation. In addition, we hope the FDA will commence appropriate regulatory actions to remove adulterated kratom products from the marketplace.

Respectfully submitted,

Dave Herman
Chairman
American Kratom Association

cc: Scott Gottlieb
Commissioner, U.S. Food and Drug Administration

Nora Volkow
Director, National Institute on Drug Abuse

Uttam Dhillon
Acting Administrator, Drug Enforcement Administration