

September 26, 2016

Chuck Rosenberg  
Acting Administrator  
U.S. Drug Enforcement Administration  
8701 Morrisette Drive  
Springfield, Virginia 22152

**Re: Docket No. DEA-442  
Emergency Scheduling of Mitragynine and 7-Hydroxymitragynine**

Dear Acting Administrator Rosenberg:

We are writing on behalf of our client, the American Kratom Association (AKA), to request that you immediately suspend the process of scheduling mitragynine and 7-hydroxymitragynine, constituents of the kratom plant, pursuant to the emergency scheduling provisions of the Controlled Substances Act (CSA).<sup>1</sup> If finalized, an emergency scheduling order would have the effect of immediately banning the production, possession, and use of a variety of natural botanical kratom products that have been commercially available and widely used by consumers in the United States over a period of decades.

The Drug Enforcement Administration's (DEA) proposed use of the emergency scheduling authority in this instance is completely unprecedented. Because it allows for a departure from formal, public regulatory processes prior to taking effect, the entry of an emergency scheduling order is intended only for the most extreme instances of harmful illicit drug use, where no other options are available to prevent "an imminent hazard to public safety."<sup>2</sup> Far from being "an imminent hazard," kratom herbal products are used routinely, safely, and responsibly by several million consumers in the United States. Never before has DEA invoked its emergency scheduling authority to take action against a natural product with a long history of safe use in the community.

Emergency scheduling is designed to give the Attorney General (acting through DEA) the ability to immediately criminalize, through schedule I control, novel synthetic or "designer" substances that quickly emerge on the illicit market. These are substances that can readily be

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<sup>1</sup> 21 USC 801 *et seq.* The CSA provides for "temporary scheduling to avoid imminent hazards to public safety," commonly referred to as the "emergency" scheduling process. We adopt that terminology here.

<sup>2</sup> 21 USC 811(h).

identified as highly addictive, are likely to be abused, and are likely to present an immediate threat of death or serious harm. Kratom is not such a substance.

As we show in this letter, kratom is a well-known, well-researched herbal substance drawn from the leaves of trees within the coffee family. The number of cases of documented harm from kratom use is remarkably low, both as an absolute matter and when considered against the extensive history of use of kratom, both inside and outside the United States.<sup>3</sup> The examples of harm are also remarkably low for a substance which, according to the DEA notice, is essentially comparable to an opioid. To the contrary, safety reports for kratom bear no resemblance in quantity and type to the reports that are the hallmark of the many potent opioid substances used and abused in the United States. Jack Henningfield, PhD, one of the world's leading experts on drugs of abuse and addiction therapy, comprehensively reviewed publicly available data on the safety of kratom and described the results as a "remarkable record of safety and low abuse risk for any substance used by millions of Americans" with "little evidence of dependence or serious adverse events and no documented kratom-caused overdose deaths."<sup>4</sup>

This is consistent with the pharmacologic properties of kratom, which make it a poor choice as an agent of abuse. Research shows that it would require a "heroic effort" to consume enough kratom to achieve the types of effects typically associated with abuse. Again, as Dr. Henningfield explains, abuse of kratom is "extremely unlikely because the pleasure derived from consumption does not appear similar in magnitude to that produced by far less costly and readily available doses of typical substances of abuse including marijuana, alcohol, stimulants, sedatives, and opioids."<sup>5</sup>

AKA recognizes that a widely used substance such as kratom cannot be considered risk-free. Thus, AKA takes very seriously DEA's concern that approximately 30 reports of fatalities have been linked to consumers who had ingested or possessed a kratom product. However, a close examination of these reports shows that there are no instances in which kratom itself was determined to be responsible for the cause of death, as further discussed in Part III.C. Because kratom does not appear to induce respiratory depression (the dominant reason why abuse or misuse of traditional opioids leads to death), as discussed in section II.B., there is good reason to question whether these reports indeed represent a valid or meaningful signal with respect to kratom. Close review of the totality of evidence points clearly in the other direction, namely, that kratom is well tolerated and relatively mild in its effects.

DEA's emergency scheduling action, if finalized, will result in material and irreparable harm to a significant number of small businesses, and will disrupt the lives of millions of consumers who have grown accustomed to using kratom safely on a regular basis. Kratom

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<sup>3</sup> See, e.g., Nat'l Forensic Laboratory Information System, *2015 Midyear Report* at 15 (2015), available at [https://www.nflis.dea/diversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLIS\\_MidYear2015.pdf](https://www.nflis.dea/diversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLIS_MidYear2015.pdf); see also discussion of poison control data in Section III.B.

<sup>4</sup> Jack E. Henningfield, Ph.D., Written Summary of Oral Testimony for the State of Wisconsin Controlled Substances Board (Aug. 14, 2015) at 3 [hereinafter Henningfield].

<sup>5</sup> *Id.* at 7.

products have a substantial consumer base in the United States, often as an alternative choice for those who wish to resist using potent prescription pain medications. Kratom is prevalent in certain ethnic communities in the United States, where it is linked by custom to the indigenous use of kratom in Southeast Asia dating back several centuries. It is also prevalent among disabled Americans, Veterans, and other consumers who find that their personal well-being is positively impacted by the use of herbal remedies. And, many use kratom products as part of a routine self-care regimen, not unlike the use of caffeine-containing products and other natural botanical products.

DEA's action will effectively punish these consumers for their health-related choice to consume a lawful product. Kratom is not a "designer" drug that is surfacing for the first time. Rather, it has been available as an herbal product through commercial channels for decades in the United States. It is well outside the intent of the emergency scheduling authority to place consumers and businesses at risk of immediate prosecution under these circumstances. The public interest and outcry could not be clearer: within weeks following DEA's emergency scheduling announcement, more than 136,000 individuals signed a petition directed to the White House in protest over the precipitous effort to schedule kratom and its active constituents.<sup>6</sup>

Thus, as we show in this letter, the proposed use of the emergency scheduling provisions in this case is unprecedented, contrary to the law and public interest, violates fundamental principles of regulatory procedure, and implicates serious constitutional questions. We respectfully ask that you immediately suspend the current emergency scheduling action. AKA and other concerned groups welcome the opportunity to work together with DEA and other federal regulators to thoroughly compile and review the evidence and, based on an appropriate, well-considered process, decide what steps may be useful to promote the safety of consumers who choose to use kratom products to support their health and well-being.

## **I. BACKGROUND**

### **A. The American Kratom Association**

AKA is a non-profit organization representing a community of responsible consumers who routinely and safely consume kratom products for improved health and well-being. The AKA provides the general public, lawmakers, and regulators with information about kratom's history of safe use, and supports scientific research to increase understanding of this natural botanical substance. AKA shares the interest of many of the affected stakeholders that the supply of kratom is safe, of appropriate quality, and marketed responsibly.

### **B. Kratom and its Active Constituents<sup>7</sup>**

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<sup>6</sup> Petition: Please Do Not Make Kratom a Schedule I Substance, <https://petitions.whitehouse.gov/petition/please-do-not-make-kratom-schedule-i-substance>.

<sup>7</sup> The DEA notice proposes to place mitragynine and 7-hydroxymitragynine, two constituents of kratom, into schedule I. For simplicity, we refer to these constituents collectively as "kratom," understanding that mitragynine and 7-hydroxymitragynine are only two of many alkaloids and other constituents that constitute the kratom plant.

Kratom (*Mitragyna speciosa*) is a deciduous tree of the coffee family (*Rubiaceae*). The kratom tree grows abundantly in tropical Southeast Asia, especially Vietnam and Malaysia. Kratom has been used for hundreds of years by the indigenous people of Southeast Asia as an herbal supplement and traditional remedy. Indeed, in that region of the world, kratom “is a part of the way of life, embedded in local custom and tradition.”<sup>8</sup> The leaves of the plant are typically chewed, steeped into a hot tea, or dried and prepared into a dosage unit or added to a beverage. Smoking and nasal insufflation of the leaves is less common, probably because of kratom’s low bioavailability or low potency.<sup>9</sup> Used in a responsible way and in moderate amounts, kratom has been reported to provide increased energy and an increased sense of well-being. Among Southeast Asian communities, kratom leaves are often used to combat diarrhea or worm infestations or to provide analgesic and antipyretic effects. The effects of kratom are generally found to be dose-related, with mild stimulant effects at lower dosages and more sedative effects at higher dosages.<sup>10</sup>

Today, millions of people in the United States consume kratom regularly, as they do other herbal supplements and traditional remedies.<sup>11</sup> Kratom sales to consumers yield revenue of approximately \$207 million in sales annually.<sup>12</sup> Data suggest that kratom sales account for approximately 20% of a total revenue of \$1.13 billion per year as reported by small business owners operating in the botanical market.<sup>13</sup> Industry estimates indicate that there are approximately 10,000 kratom vendors operating in the United States market. In response to a recent industry survey, respondents reported that they employ upwards of 2,500 people in small businesses specializing in kratom products.<sup>14</sup>

Kratom has a long history of use with comparatively few reports of confirmed adverse events. Despite its widespread use in Southeast Asia, serious adverse events have rarely been associated with kratom usage in the region.<sup>15</sup> Likewise, in the United States, there have been few reported serious side effects associated with kratom use and no reported deaths directly

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<sup>8</sup> Satariya Trakulsrichai et al., *Pharmacokinetics of Mitragynine in Man*, 9 *Drug Design, Dev. and Therapy* 2421, 2422 (2015).

<sup>9</sup> Henningfield at 2. Mitragynine’s bioavailability is approximately 3% when taken orally. *Id.* at 3; Catherine Ulbricht, Pharm.D. et al., *An Evidence-Based Systematic Review of Kratom (Mitragyna speciosa) by the Natural Standard Research Collaboration*, 10 *J. Dietary Supplements*, 152, 163 (2013).

<sup>10</sup> Henningfield at 2; Trakulsrichai et al. at 2421.

<sup>11</sup> Henningfield at 3.

<sup>12</sup> Data compiled by the Botanical Education Alliance through a survey sampling of businesses operating in the kratom industry; September 2016. The data is accessible at [https://www.botanical-education.org/wp-content/uploads/2016/09/BEA-Economic-Impact-Report\\_V3.pdf](https://www.botanical-education.org/wp-content/uploads/2016/09/BEA-Economic-Impact-Report_V3.pdf).

<sup>13</sup> *Id.*

<sup>14</sup> *Id.*

<sup>15</sup> Henningfield at 2; Ulbricht et al. at 157; Trakulsrichai et al. at 2422.

attributable to the substance.<sup>16</sup> A former senior scientist for the National Institute on Drug Abuse (NIDA) and one of the world's leading experts on drugs of abuse, Jack Henningfield, PhD, describes kratom as having a "remarkable record of safety."<sup>17</sup>

The relative safety of kratom is consistent with several key clinical and pharmacologic properties of the substance. First, as demonstrated through numerous studies in animals, kratom consistently exhibits very low toxicity. In multiple animal studies, when tested at extremely high exposure levels, kratom was not shown to induce death or other significant signs or signals of toxic effects.<sup>18</sup>

Second, kratom's unique pharmacology distinguishes it from classic opioids with addictive properties, such as codeine, fentanyl, and morphine. Although mitragynine binds to the mu-opioid receptors in the brain like opioids, several of the other major alkaloids in kratom demonstrate competing antagonist activity at the opioid receptors.<sup>19</sup> For example, kappa agonism "seems to attenuate reinforcement and produce aversion." Thus, unlike opioid products, this distinct pharmacological behavior limits any possible "high" that can be achieved through kratom use and significantly reduces any potential for abuse.<sup>20</sup>

Third, kratom exhibits very low bioavailability—only about 3% when taken orally. For comparison, oral morphine shows bioavailability between 20 and 25%,<sup>21</sup> fentanyl ranges from 50% to almost 70%,<sup>22</sup> and oral codeine is approximately 90% bioavailable.<sup>23</sup> Kratom's low bioavailability reduces the extent to which any effect, positive or negative, can be achieved, and substantially reduces the possibility of overdose because a user would need to ingest an overly large (and likely aversive) amount to achieve a euphoric "high." As described by Walter C.

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<sup>16</sup> See Edward W. Boyer et al., *Self-treatment of opioid withdrawal using Kratom (Mitragynia speciosa korth)*, ADDICTION 103(6); 1048-50 (date) ("Although mitragynines agonize mu-opioid receptors, respiratory depression, coma, pulmonary edema and death have not, to our knowledge, been associated with human Kratom ingestion."). See section III.A.2, *infra*, for a more thorough discussion of the adverse effects and deaths claimed to be attributable to kratom.

<sup>17</sup> Henningfield at 3.

<sup>18</sup> See, e.g., M.S.A. Kamal et al., *Acute toxicity study of standardized Mitragyna speciosa Korth aqueous extract in Sprague Dawley rats*, 1 J. Plant Stud. 120-129 (2012); A. Sabetghadam et al., *Subchronic exposure to Mitragynine, the principal alkaloid of Mitragyna speciosa, in rats*, 146 J. Ethnopharmacol. 815-23 (2013); Henningfield at 4 (citing studies).

<sup>19</sup> Andrew C. Kruegel et al., *Synthetic and Receptor Signaling Explorations of the Mitragyna Alkaloids: Mitragynine as an Atypical Molecular Framework for Opioid Receptor Modulators*, 138 J. Am. Chem. Soc. 6754, 6762 (2016).

<sup>20</sup> *Id.* at 6762.

<sup>21</sup> P.J. Hoskin et al., *The Bioavailability and Pharmacokinetics of Morphine after Intravenous, Oral and Buccal Administration in Healthy Volunteers*, 27 J. Clin. Pharmacol. 499 (1989).

<sup>22</sup> Abstral Clinical Pharmacology Review, NDA 22510 (Mar. 11, 2010); see also M. Darwish et al., *Absolute and Relative Bioavailability of Fentanyl Buccal Tablet and Oral Transmucosal Fentanyl Citrate*, 47 J. Clin. Pharmacol. 343 (2007).

<sup>23</sup> See, e.g., Clinical Pharmacology and Biopharmaceutics Review at 5, NDA 202245, Codeine Sulfate oral solution (Dec. 6, 2010).

Prozialeck, a professor of pharmacology at Midwestern University who has studied kratom extensively, “[T]he amount [of kratom] that a person has to take in to get any severe effects is ridiculously high. You’re talking 10 to 15 grams of raw leaf. Most people who are using kratom for pain management don’t take that much. Most people can’t take that much.”<sup>24</sup> Indeed, an intoxicating effect can be achieved with lower doses of dextromethorphan or nutmeg.<sup>25</sup> Finally, unlike potent opioid substances, kratom does not carry a high risk of respiratory depression, which is generally the cause of death in cases of opioid overdose.<sup>26</sup> The “[r]espiratory depressant effects appear substantially lower than those produced by opioids and this would be consistent with the absence of verified kratom caused overdose death.”<sup>27</sup> Moreover, because kratom does not produce the euphoric “high” that drives addiction to opioids and other drugs, it is less likely to be abused at high doses, also lessening any risk of respiratory depression.

### C. The DEA Notice

On August 31, 2016, DEA published a notice in the Federal Register announcing its intent to use its scheduling authority to control mitragynine and 7-hydroxymitragynine in schedule I.<sup>28</sup> The agency claimed such action is “necessary to avoid an imminent hazard to the public safety.”<sup>29</sup> In reaching this conclusion, the agency asserted that mitragynine and 7-hydroxymitragynine have a high potential for abuse, no currently accepted medical use in the United States, and a lack of accepted safety for use under medical supervision.<sup>30</sup>

The August 31 announcement provides 30 days’ notice of DEA’s plan to place mitragynine and 7-hydroxymitragynine in schedule I. If a final order follows, placing mitragynine and 7-hydroxymitragynine into schedule I of the CSA for a period that can last up to three years, all of the administrative, civil, and criminal sanctions associated with schedule I controlled substances would immediately apply to kratom.<sup>31</sup> A final order would affect the millions of Americans who consume kratom safely and responsibly as part of their healthy

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<sup>24</sup> Nick Wing, *Some Say Kratom Is A Solution to Opioid Addiction. Not If Drug Warriors Ban It First*, Huffington Post, updated Sept. 7, 2016, 8:38 am, [http://www.huffingtonpost.com/entry/kratom-ban-drug-policy\\_us\\_56c38a87e4b0c3c55052ee3f](http://www.huffingtonpost.com/entry/kratom-ban-drug-policy_us_56c38a87e4b0c3c55052ee3f).

<sup>25</sup> Henningfield at 6.

<sup>26</sup> See Kruegel at 6754-55 (“Unfortunately, acute [mu-opioid receptor] activation is also associated with serious side effects, including respiratory depression, constipation, sedation, nausea, and itching. At sufficiently high doses, the evoked respiratory depression may be fatal.”).

<sup>27</sup> Henningfield at 6; see also U.S. Patent No 201002 [0110] (“Toxicity studies of lyophilized Kratom extraction into water have failed to produce respiratory depression. Toxicity studies using mitragynine performed in the rat failed to identify respiratory depression, even at doses of 800 mg/kg administered via intraperitoneal dosing.” (References omitted.)).

<sup>28</sup> 81 FR 59929-34.

<sup>29</sup> *Id.* at 59929.

<sup>30</sup> *Id.* at 59930.

<sup>31</sup> 81 FR at 59933.

lifestyles along with other plant-derived products like coffee, guarana, and kola nut, as well as the many small businesses providing kratom products in the United States.

## II. STATUTORY FRAMEWORK FOR SCHEDULING

### A. The Scheduling Process

A centerpiece of the CSA is a carefully constructed, multi-factorial administrative process that allows a substance to be added to a CSA schedule only after a detailed analysis of data and evidence relating to a substance's medical use, potential for abuse, and dependence liability.<sup>32</sup> Reflecting the significance of the contemplated action, the process is measured and deliberate, with complementary analyses required from two federal departments and three federal agencies, followed by a public rulemaking in which all interested parties may participate. Moreover, the two lead participants in the process – DEA and the Department of Health and Human Services (HHS) – act together to provide a series of checks and balances, with the HHS analysis (typically conducted jointly by FDA and NIDA) binding on DEA as to scientific and medical matters. If HHS recommends against scheduling, the proposed action cannot occur. These multiple layers of process and safeguards are required because Congress recognized the extraordinary consequences of scheduling a substance.

Specifically, the process to schedule a substance begins when DEA requests a scientific and medical evaluation from HHS,<sup>33</sup> which must include analysis of the following eight factors:

- The substance's actual or relative potential for abuse;
- Scientific evidence of its pharmacological effect, if known;
- The state of current scientific knowledge regarding the drug or other substance;
- Its history and current pattern of abuse;
- The scope, duration, and significance of abuse;
- What, if any, risk there is to the public health;
- Its psychic or physiological dependence liability; and
- Whether the substance is an immediate precursor of an already-controlled substance.<sup>34</sup>

After consideration of the eight factors, HHS makes a recommendation as to the appropriate schedule for the substance. Provided HHS recommends scheduling, DEA then performs its own analysis of the eight factors. If it determines that substantial evidence of a potential for abuse exists, DEA next initiates proceedings for control of the substance through rulemaking on the

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<sup>32</sup> 21 USC 811(b), (c).

<sup>33</sup> *Id.* at 811(b).

<sup>34</sup> *Id.* at 811(b), (c).

record, with an opportunity for public comment and an opportunity for a hearing pursuant to the rulemaking procedures set out in the Administrative Procedures Act (APA).<sup>35</sup>

## **B. Emergency Scheduling**

The CSA authorizes the Attorney General, acting through DEA, to exercise emergency scheduling authority when the Administrator finds such scheduling “is necessary to avoid an imminent hazard to the public safety.”<sup>36</sup> The expedited procedure permits DEA to bypass the normal scheduling procedure, in rare instances, on an “emergency” basis, without the analysis, findings, and opportunity for public participation otherwise required by the CSA.<sup>37</sup> Despite the departure from the typical process and the “temporary” nomenclature, the emergency scheduling order has lasting consequences: it is effective for two years, with the option to extend it for an additional year.<sup>38</sup>

The emergency scheduling authority was added to the CSA in 1984 at DEA’s request.<sup>39</sup> The Act does not define “imminent hazard,” but the meaning was discussed by Congress and DEA during the drafting and consideration of the new statutory provision. When asked by legislators what was meant by “imminent hazard,” then-Administrator Mullen explained:

The use of the term “imminent hazard to the public safety” is based on several factors. The “imminent hazard” implies a need for immediate response to a drug trafficking and abuse situation that has occurred with such rapidity and with insufficient warning that normal control mechanisms would result in a large number of deaths and injuries or the continuance of an uncontrolled trafficking situation. ... The burden would be on the Government to prove that such an urgency exists and that the public safety would be jeopardized during the period that a drug would remain uncontrolled during routine scheduling action.<sup>40</sup>

As an example of a case of imminent harm, the Administrator cited the synthetic drugs being produced in “clandestine laboratories”:

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<sup>35</sup> *Id.* at 811(a), (b).

<sup>36</sup> *Id.* at 811(h)(1).

<sup>37</sup> *Id.* at 811(h).

<sup>38</sup> *Id.* at 811(h)(2). The order is vacated once the substance is scheduled through the normal administrative scheduling process. *Id.* at 811(h)(5).

<sup>39</sup> See Pub. L. 98-473, Tit. II, §§ 508, 509(a) (Oct. 12, 1984); see also *Diversion of Prescription Drugs to Illegal Channels and Dangerous Drug Diversion Control Act: Hearing on H.R. 4698 Before the H. Comm. on the Judiciary, 98<sup>th</sup> Cong. 401-04 (1984)* (letter of Francis M. Mullen, Jr., Administrator, DEA) (“Mullen Letter”).

<sup>40</sup> Mullen Letter at 401.



Newly synthesized drugs or uncontrolled analogs of existing drugs such as PCP [phencyclidine] and fentanyl are being produced and abused. They can cause widespread deaths and injuries in a very short period of time following their synthesis.<sup>41</sup>

He then discussed the examples of cyclohexamine (PCE) and phenylcyclohexylpyrrolidine (PHP), analogs of PCP that produce similar effects. When controls of PCP were increased, non-controlled analogs appeared in the illegal drug trade. Although the analogs were sold on the streets as PCP and carried the same risks, law enforcement could not prosecute the drug dealers because the analogs were not scheduled substances.<sup>42</sup> That experience, and similar experiences with other synthesized analogs of illicit drugs, led to the creation of the expedited scheduling process. Administrator Mullen emphasized to Congress, however, that the new authority would be used judiciously, “infrequently,” and “*only in the most extreme cases* where the time needed for the routine scheduling process would work to the detriment of the public safety.”<sup>43</sup>

In that same vein, the legislative history reflects Congress’s intent that the emergency scheduling provision would be used for extreme emergencies in which analogs of currently controlled substances had appeared to rapidly to be addressed by the ordinary scheduling procedure. For example, the Senate Report on the bill stated: “The new emergency control authority [codified at 21 USC 811(h)] is designed to allow the Attorney General to respond quickly to protect the public from drugs of abuse that *appear* in the illicit traffic *too rapidly to be effectively handled* under the lengthy routine control procedures.”<sup>44</sup> In floor debate, the members of Congress that addressed the emergency scheduling provision stated that it was “an expedited procedure to control chemicals that *mimic the effects* of hallucinogenic drugs, such as PCP”<sup>45</sup> and “will enable us to rapidly control newly developed chemicals, sometimes called designer drugs, that are similar to controlled drugs.”<sup>46</sup>

More recently, Congress shed more light on the meaning of “imminent hazard” when it defined similar language in another part of the CSA: Section 824(d) authorizes DEA to immediately suspend an entity’s registration if the Administrator finds that there is an “imminent danger to the public health or safety.”<sup>47</sup> Congress clarified that for purposes of the subsection,

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<sup>41</sup> *Id.* Other examples provided by Administrator Mullen as appropriate for emergency scheduling included analogs of heroin, amphetamine, and methaqualone, among many others. *Diversion of Prescription Drugs to Illegal Channels and Dangerous Drug Diversion Control Act: Hearing on H.R. 4698 Before the H. Comm. on the Judiciary*, 98<sup>th</sup> Cong. 463-65 (1984) (statement of Maurice O. Bectel, interim president, American Pharmaceutical Association).

<sup>42</sup> Mullen Letter at 402.

<sup>43</sup> *Id.* at 402 (emphasis added).

<sup>44</sup> S. Rep. No. 98-225 at 264-65 (emphasis added).

<sup>45</sup> H. Rec. 9679 (Rep. Hughes) (emphasis added).

<sup>46</sup> H. Rec. 9682 (Rep. Rodino)

<sup>47</sup> 21 USC 824(d).

the phrase ‘imminent danger to the public health or safety’ means that, due to the failure of the registrant to maintain effective controls against diversion or otherwise comply with the obligations of a registrant . . . , *there is a substantial likelihood of an immediate threat that death, serious bodily harm, or abuse of a controlled substance will occur in the absence of an immediate suspension of the registration.*<sup>48</sup>

Accordingly, the exercise of DEA’s emergency scheduling authority is appropriate only where, in the absence of that scheduling, *there is a substantial likelihood of an immediate threat that death, serious bodily harm, or abuse will occur.*

In its process of determining whether an imminent hazard to the public health exists, DEA must explicitly consider three factors:

- (1) the substance’s history and current pattern of abuse
- (2) the scope, duration, and significance of abuse and
- (3) what, if any, risk there is to the public health.<sup>49</sup>

The analysis must also include the substance’s actual abuse, diversion from legitimate channels, and clandestine importation, manufacture, or distribution.<sup>50</sup>

### **III. KRATOM DOES NOT MEET THE LEGAL STANDARD FOR EMERGENCY SCHEDULING UNDER THE CSA**

Section 811(h) of the CSA was created to enable DEA to respond to newly synthesized versions of well-known drugs of abuse with a risk profile so extreme that, absent emergency action, there would be large numbers of deaths and serious injuries in the community. Emergency scheduling is a vital law enforcement tool to be used in the face of a clear and imminent danger to public safety. The urgency of the situation allows DEA to take action ahead of its usual open, public process. The emergency scheduling authority reflects a careful policy balance, in which public safety is allowed to take priority over public process based on extraordinary circumstances.

As shown below, the evidence compiled by DEA falls well short of the very high burden DEA must clear in order to justify the need for taking an emergency scheduling action. Kratom use is ancient, not “rapidly” emerging. Kratom is not a new “designer drug” concocted to avoid existing DEA controls; it is a natural botanical substance openly marketed primarily as a natural-source consumer product. Kratom is not intensely reinforcing, leading to destructive behavior. In fact, the evidence is far more compelling that kratom is a staple of self-care that allows individuals to lead their lives productively and without unnecessary reliance on more harmful

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<sup>48</sup> *Id.*

<sup>49</sup> 21 USC 811(h)(3).

<sup>50</sup> *Id.*

substances. And, when considered against the large “denominator” of usage both in the United States and globally, over a long period of time, the quantity and type of adverse events reported for kratom is indeed remarkable – it is remarkable for the relatively *low* volume of reports and incidents, which as a whole are in line with many other marketed supplements and natural products.

**A. Kratom’s History and Current Pattern of Abuse, If Any, Does Not Support the Need for Emergency Scheduling**

Having been consumed world-wide for centuries and used in the United States for many years, the use of kratom in the United States could hardly be considered a new phenomenon. The small businesses that provide kratom to Americans who consume the plant for its perceived health benefits do not constitute “an uncontrolled trafficking situation.” And the safe and responsible use of kratom by consumers as they use other natural botanical products does not constitute “abuse.” Most importantly, kratom does not have – as DEA asserts in the notice – a “high potential for abuse.”

The term abuse is not defined in the CSA, but the legislative history of the CSA provides guidance for analyzing a substance’s abuse for purposes of scheduling under the CSA.<sup>51</sup> Considerations include: evidence that individuals are taking the substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or the community; diversion of the substance from legitimate channels; evidence that individuals are taking the substance on their own initiative rather than on the basis of medical advice from a practitioner; and whether the substance is so related in its action to a drug already listed as having a potential for abuse to make it likely that the substance will have the same potential for abuse.<sup>52</sup> Together, these considerations demonstrate that kratom does *not* demonstrate a high potential for abuse similar to fentanyl or oxycodone – but, rather, shares characteristics of unscheduled, naturally-derived substances such as caffeine.

First, there is little evidence that individuals are taking kratom in amounts sufficient to create a hazard to their health or to the safety of others. If that were the case, we would expect to see many cases of serious adverse events and overdose deaths. Yet, though more than one million people in Thailand alone use kratom regularly,<sup>53</sup> fewer than 100 serious adverse events related to kratom use have been reported *globally*, and most were likely caused by the co-administration of other substances.<sup>54</sup> Likewise, in the United States, there have been *no* reported overdose deaths attributable to kratom alone, as discussed in detail below. Moreover, there is no evidence that kratom use is associated with an increased incidence of traffic accidents, acts of violence, unemployment, criminal behavior, or other negative consequences to indicate that it is

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<sup>51</sup> Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970) reprinted in U.S.C.C.A.N. 4566, 4603

<sup>52</sup> See, e.g., 81 FR 53688 (August 12, 2016) (denying petition to reschedule marijuana).

<sup>53</sup> Henningfield at 3.

<sup>54</sup> *Id.*

being used at levels that cause harm to the community. Indeed, many kratom consumers assert that kratom has enabled them to once again be active, contributing members of their communities.

Second, kratom has been available as a natural botanical product for decades in the United States through health-food stores and other legitimate businesses. There is no evidence that kratom has been diverted from these legitimate sources into an illicit drug market. Specifically, kratom is not being diverted in the ways Congress contemplated when it drafted the CSA: from legitimate sources through sham operations that function as covers for the illegal distribution of scheduled drugs or by “underground chemists” seeking to evade the controls of applicable law.<sup>55</sup> The question of “diversion” simply does not apply to kratom, a botanical product that has been sold openly in legitimate businesses for many years.

Third, there is little information regarding the extent to which individuals are taking kratom on their own initiative rather than on the basis of medical advice from a practitioner because kratom is a product that is available through legal channels without a prescription, similar to many other botanical products. The fact that many consumers may, on their own initiative, choose to purchase kratom through a legal channel of commerce does not establish that the product is being abused.

Fourth, kratom is not related to a drug already listed as having a potential for abuse in such a way that would suggest kratom would have the same potential for abuse. Although kratom shares certain characteristics with classic opioids, including certain opioid-receptor activity, it is equally distinguishable from classic opioids in a number of crucial respects. Perhaps most importantly, kratom does not exhibit the binding profile associated with the reinforcing qualities that lead to opioid addiction and abuse. Mitragynine<sup>56</sup> binds to several non-opioid receptors, and demonstrates both agonist and antagonist effects at the opioid receptors, limiting the “high” that can be achieved with kratom and, with it, the potential for abuse.<sup>57</sup> Kreugel et al. found that mitragynine “acted as a partial agonist” for the mu-opioid receptor, but did not bind the delta-opioid receptor or the kappa-opioid receptor.<sup>58</sup> In fact, at the kappa receptor, mitragynine “was a competitive antagonist, fully inhibiting the activity of the reference agonist.”<sup>59</sup> Mitragynine was also an antagonist at the delta opioid receptor, although with lower potency than at the kappa receptor.<sup>60</sup>

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<sup>55</sup> H. Rep. 98-835 (June 12, 1984) at 7-9.

<sup>56</sup> *See, e.g.*, Kreugel et al. at 6756 (reporting that it was “not possible to isolate any measureable quantity” of 7-hydroxymitragynine).

<sup>57</sup> *Id.* at 6754.

<sup>58</sup> *Id.* at 6756.

<sup>59</sup> *Id.* (citation omitted).

<sup>60</sup> *Id.*

Although 7-hydroxymitragynine has been characterized in the literature as the more potent alkaloid, it is usually present in kratom at levels below the limit of detection and is unlikely to be responsible for any effects of the plant on users of kratom. Kreugel et al. stated that “only trace quantities of [7-hydroxymitragynine] were observed (by mass spectrometry) in our extractions of the raw plant material, and it was not possible to isolate any measurable quantity of this derivative. Therefore, it is doubtful that this alkaloid is a universal constituent of all [kratom] preparations and is unlikely to generally account for the psychoactive properties of this plant.”<sup>61</sup> Similarly, Dr. Henningfield noted that 7-hydroxymitragynine is a “minor constituent” of kratom leaves, only 2% of the crude base, and in common kratom products, 7-hydroxymitragynine has “not [been] present... at detectable levels, and therefore does not present a safety concern.”<sup>62</sup> Regarding other constituents of kratom, Kreugel et al. found that “[t]he other major natural alkaloids... showed no measurable agonist activity at any of the human opioid receptors” even at high concentrations.<sup>63</sup>

In addition, recent research at Columbia University is adding to the weight of evidence demonstrating that the primary constituents of kratom, mitragynine and 7-hydroxymitragynine, have significantly different pharmacology profiles from traditionally abused opioids. The substance’s selective bias towards only a single pathway – the G-protein pathway – helps explain why there is *no evidence* of respiratory depressions associated with kratom use, and the partial agonist activity exhibited by mitragynine and 7-hydroxymitragynine supports the lack of reinforcing effect ordinarily associated with classic opioids.<sup>64</sup> Functionally selective agonists, like mitragynine, are known to produce reduced side effects, and in particular, “agonists biased toward G protein signaling... display less respiratory depression, tolerance development, and constipation.”<sup>65</sup> In sum, mitragynine’s specificity to the mu-opioid receptor, and only partial affinity for that receptor, limits its ability to generate euphoria. Mitragynine’s reinforcing effects are further limited by its activity as an opioid antagonist to the kappa and delta receptors. And finally, its functional selectivity for G protein signaling indicates that it is unlikely to generate the respiratory depression present in common opioids. The result is that kratom’s constituents show vast chemical differences from opioids and prompt effects in the body unlike opioid painkillers.

Indeed, rather than resembling the classic opioids, kratom’s pharmacological action is often described as similar to caffeine. According to Dr. Henningfield, “in many respects, the factors that appear important in sustaining kratom use appear more similar to those that sustain dietary caffeine use, namely to better manage fatigue and daily life demands and provide mild effects considered enhancing to quality of life.”<sup>66</sup> Moreover, many common products including

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<sup>61</sup> *Id.*

<sup>62</sup> Henningfield at 2.

<sup>63</sup> Kreugel et al. at 6756-57.

<sup>64</sup> *Id.* at 6757.

<sup>65</sup> *Id.*

<sup>66</sup> Henningfield at 7.

caffeine such as soda, coffee, and over-the-counter medicines contain enough caffeine in a single unit to produce reinforcement,<sup>67</sup> while one would need to consume doses “far higher than those commonly ingested by people in the United States” to achieve reinforcement through kratom.<sup>68</sup>

Kratom also differs from classical opioids in terms of its very low bioavailability, as only 3% is bioavailable when taken orally. This is a fraction of the bioavailability of scheduled opioids such as morphine, fentanyl, and codeine, with oral bioavailability of approximately 20-25%, 50-70%, and 90%, respectively. Dr. Henningfield describes the oral absorption of mitragynine as “slow, prolonged and [] incomplete.”<sup>69</sup> Kratom’s exceptionally low bioavailability limits the extent to which a user could experience a “high,” reduces the possibility of overdose, and limits reinforcement. These pharmacological characteristics of kratom suggest that it is a very poor candidate for abuse, and this is reflected in the absence of actual abuse observed in the United States.

The current patterns of use do not reflect the telltale patterns of abuse associated with substances that carry a high and dangerous level of abuse liability. Kratom presents a wholly different picture. Several million law-abiding consumers use kratom just as they would any other botanical or natural remedy they see on the commercial market. There is little to no evidence of experimentation with alternative routes of administration; with criminal activity associated with its production and use; or with debilitating reinforcing effects that pose a threat to the community or to the individual. Indeed, there are far more reports of kratom users being able to lead normal lives, than reports of quintessential destructive behaviors associated with highly abused substances. This picture is not by happenstance. As shown throughout this letter and the body of supporting evidence, kratom does not exhibit the properties of classic opioids that lead the substances in that class to be highly abused.

### **B. The Scope, Duration, and Significance of Abuse of Kratom, if Any, Does Not Support the Need for Emergency Scheduling**

DEA is required by statute to amass and assess the evidence with regard to the “scope, duration, and significance of abuse” of a substance proposed for emergency scheduling. While the DEA Notice includes evidence on the use of kratom, it is far from clear that material gathered by DEA represents evidence of *abuse* of kratom. The DEA analysis is fundamentally flawed because the body of evidence presented by DEA does not distinguish between true abuse, within the meaning of the CSA, and “non-abusive,” ordinary-course use of kratom by law-abiding citizens. A critical piece of the analysis that DEA failed to address is that kratom has been available for many years through lawful channels. DEA assumes, instead, that any documented use of kratom is *per se* abuse. That assumption, which informs DEA’s entire reading of the record, is flawed. Kratom has been available for many years without being considered an

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<sup>67</sup> *Id.* at 9-12.

<sup>68</sup> *Id.* at 6.

<sup>69</sup> *Id.* at 8.

unlawful substance. DEA conflates the good faith use of kratom by law-abiding consumers with abuse, rendering its Notice and the basis for its actions clearly erroneous.

To begin, the sources relied upon by DEA cannot distinguish between the lawful purchase and consumption of a widely used consumer product on the one hand, and illicit abuse of a product that threatens the public health on the other. In addition, some of the data sources aggregate data internationally and do not distinguish between domestic and international use, or have been described by DEA itself as unreliable, further undercutting the ability to distinguish between use and abuse. As a result, these sources cannot support the finding that kratom presents “a substantial likelihood of an immediate threat that death, serious bodily harm, or abuse will occur.”<sup>70</sup>

For example, the agency cites data from the System to Retrieve Information from Drug Evidence (STRIDE), together with data from a commercial laboratory information management system, indicating that during a 10-year period ending in March 2016, there were 293 records related to kratom and/or mitragynine.<sup>71</sup> Yet, DEA’s own website states that STRIDE data is “unvalidated” and “is not a representative sample of drugs available in the United States, but reflects all evidence submitted to DEA laboratories for analysis, from both domestic and foreign sources.”<sup>72</sup> The emergency scheduling of a substance cannot be based on such unvalidated data. Moreover, the data only show that kratom samples were analyzed in laboratories – they do not speak to the reasons for the analysis and cannot discriminate between legitimate use and any potential abuse. Taken together, the reports are inadequate and unreliable to support any conclusion other than that kratom is used by a number of consumers around the world.

DEA’s reliance on data from poison control centers is also problematic as the data do not demonstrate imminent harm or a substantial likelihood of an immediate threat of abuse, as is required to meet the standard in the CSA for emergency scheduling. DEA claims that poison control records exhibit the abuse of kratom because they showed that people were using kratom in ways that caused serious adverse events; yet careful analysis of these calls by the Centers for Disease Control (CDC) shows that the serious adverse events were strongly associated with consumption of substances other than kratom, rendering any conclusion about abuse, rather than use, impossible to draw from the poison control data.

DEA’s proposed scheduling notice and accompanying three-factor analysis rely on a Weekly Morbidity and Mortality Report published on CDC’s website for a summary of poison control center reports.<sup>73</sup> As explained above, DEA quotes the report’s finding that during a six-year period ending in December 2015, poison control centers in the United States received 660

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<sup>70</sup> 21 USC 824(d).

<sup>71</sup> 81 FR at 59931.

<sup>72</sup> <https://www.dea.gov/resource-center/stride-data.shtml>.

<sup>73</sup> DEA’s source was Mehruba Anwar, Royal Law, and Josh Schier, *Notes from the Field: Kratom (Mitragyna speciosa) Exposures Reported to Poison Centers – United States, 2010-2015*, 65 CDC’s Morbidity and Mortality Weekly Report 748 (2016) [hereinafter MMWR].

calls related to kratom exposure, representing a tenfold increase during that period.<sup>74</sup> The authors report that the source of their data is the National Poison Data System (NPDS), a database of information logged by the nation's regional poison control centers.<sup>75</sup> Yet the past six years of annual reports from NPDS do not list any cases involving exposure to kratom, mitragynine, or 7-hydroxymitragynine.<sup>76</sup> A careful examination of CDC's methods reveals the reason for the discrepancy. The NPDS annual reports focus on single substance exposures by reporting demographic data, reasons, and outcome for reported single-substance exposure events. Apparently, single substance events involving kratom were sufficiently infrequent that NPDS included kratom in its general category of "Other Single Ingredient Botanicals," rather than listing kratom as a separate category as it does for ten other botanical dietary supplements.<sup>77</sup> In contrast, CDC's study, and resulting 660 number, considers all reports in which kratom was one substance reported, regardless of how many other substances were also reported.<sup>78</sup> That is why the authors note that many of the reports also included ingestion of "ethanol, other botanicals, benzodiazepines, narcotics, and acetaminophen"<sup>79</sup> – which may have been responsible for the reported adverse effects. Indeed, the authors themselves note "a significant association between severity of outcome and multiple versus single exposure ( $p < 0.001$ )," indicating that more serious adverse events were almost invariably associated with the ingestion of other products.<sup>80</sup> The fact that, to a high degree of certainty, ingesting kratom *without* known narcotics was associated with fewer adverse events, and less severe adverse events when they did occur, provides strong evidence that other substances were driving the serious adverse event reports.

When calls for multi-substance exposure are excluded, a third of the reports are eliminated, and the data set is limited to 428 calls regarding kratom alone over six years.<sup>81</sup> That number must be considered within the context of the millions of Americans regularly consuming kratom with no reported adverse events. In addition, the number of poison control calls regarding kratom is substantially lower than the number of calls regarding other uncontrolled substances, including caffeine (23,203 reports in the past six years), essential oils (66,300 reports in the past six years), and other widely available household substances.<sup>82</sup> Even restricting analysis to other botanical dietary supplements, nearly every common, legally marketed botanical dietary supplement for which data are available from NPDS were the subject of large numbers of single-substance reports to poison control centers over the last six years: Echinacea

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<sup>74</sup> 81 FR 59932.

<sup>75</sup> See MMWR.

<sup>76</sup> *Id.*

<sup>77</sup> Annual Reports of the American Association of Poison Control Centers' National Poison Data System 2009-2014 (hereinafter AAPCC data) (the most recent six years for which reports were available).

<sup>78</sup> MMWR.

<sup>79</sup> *Id.*

<sup>80</sup> *Id.*

<sup>81</sup> *Id.*

<sup>82</sup> AAPCC data 2009-14. Caffeine totals include only single-entity caffeine products; they do not include products containing caffeine, such as energy drinks, alcoholic drinks, or multi-ingredient drugs containing caffeine.



(1,464 case mentions, with 1,149 single-substance reports), Ginkgo Biloba (681 cases, 413 single-substance reports), St. John's Wort (1,173 cases, 717 single-substance reports), Valerian (1,499 cases, 778 single-substance reports), Kava Kava (342 cases, 196 single-substance reports), Ginseng (638 cases, 412 single-substance reports) and Yohimbe (1,246 cases, 985 single-substance reports).<sup>83</sup> Moreover, many of these substances show equivalent or greater reinforcing activity. St. John's Wort, Valerian, and Kava Kava are all known to have "reinforcing effects" and act as sedatives,<sup>84</sup> and ginseng included one reported death in 2011,<sup>85</sup> yet these substances remain widely available and legally marketed botanical products. In summary, the millions of American users of single-substance kratom called poison control centers about half as often as users of Echinacea, St. John's Wort, Valerian, or Yohimbe, and about as often as users of ginkgo biloba, and ginseng. People who used only kratom were far less likely to report serious adverse events. The poison control data simply do not distinguish kratom from other commonly marketed botanical products, and the DEA cannot conclude that the poison control data are indicative of abuse, rather than lawful consumption.

The DEA's reliance on data from poison control centers and unavailable emails on file at DEA is as telling for the data it omits as the data it includes, for it omits data from the sources that could differentiate abuse from use. Nowhere does DEA rely on the scientific, epidemiological, and public health sources that normally undergird the assertion that a substance poses a high potential for abuse, let alone an imminent public health threat. When evaluating whether a substance has a history or current pattern of abuse, DEA ordinarily relies on a number of national surveys and data sources. These sources include the National Survey on Drug Use and Health,<sup>86</sup> Monitoring the Future,<sup>87</sup> the Drug Abuse Warning Network,<sup>88</sup> and Treatment Episode Data Sets,<sup>89</sup> among others.<sup>90</sup> These databases report the age of users, the frequency of use, involvement with the criminal justice system, use in combination with illicit substances, use leading to emergency department visits, and use patterns consistent with addiction. In addition, data from these established sources are able to document the use of a substance in the population as a whole, among both occasional and frequent users, including those who do and do not experience adverse events. Again, DEA did not cite to any of these databases to support its

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<sup>83</sup> *Id.*

<sup>84</sup> Henningfield at 8.

<sup>85</sup> AAPCC data 2011.

<sup>86</sup> An annual nationwide survey involving interviews with approximately 70,000 individuals in the United States aged 12 and older.

<sup>87</sup> An annual survey of 50,000 8th, 10th, and 12th grade students with annual follow-up questionnaires mailed to a sample of each graduating class for a number of years after initial participation.

<sup>88</sup> A public health surveillance system that monitored drug-related visits to hospital emergency departments and drug-related deaths until 2011.

<sup>89</sup> A database maintaining records for 1.5 million substance abuse treatment admissions annually by aggregating data collected by states. Facilities that receive state alcohol or drug agency funds (including federal block grant funds) report data into the system.

<sup>90</sup> *See, e.g.*, 81 FR 53688, 53702-04 (Aug. 12, 2016) (DEA scheduling decision on marijuana making use of these sources to determine history and current pattern of marijuana abuse).

finding that the emergency scheduling of kratom is appropriate. These databases could have provided the information that DEA's notice is sorely lacking: statistics that differentiate between legitimate use and abuse and that indicate the presence or absence of risk factors that affect the public health.

The only other data cited in the letter as evidence of abuse potential are email correspondence with three laboratories that are not available to the public for analysis. DEA notes that a laboratory in Pennsylvania reported 31 positive results for kratom exposure in 11 months, a laboratory in Florida reported 274 positive results in 10 months, and a third laboratory in California reported 555 positive results in 15 months, and from these data points concludes that abuse of kratom is increasing.<sup>91</sup> Because these data are drawn from different laboratories and different time periods, they are not even sufficient to show whether the *use* of kratom is increasing, let alone the *abuse* of kratom. Moreover, there is no indication of why these analytical laboratories were including kratom components in their screening, but even if the number of tests detecting kratom is increasing, such a result should not be surprising given the widespread legitimate use of the product. Again, such data is not quantitatively or qualitatively the sort of information that should be used to support a finding of abuse sufficient to warrant emergency scheduling.

In sum, the data presented by DEA is consistent with the safe use of a botanical substance in good faith by law abiding consumers. DEA makes much of the fact that callers to poison control centers report "intentional exposure" to kratom.<sup>92</sup> However, consumers regularly intentionally and appropriately expose themselves to botanical products. DEA likewise cites as a risk factor the fact that "abusers obtain kratom" from commercial sources;<sup>93</sup> again, however, the evidence does not show that customers purchasing kratom are abusing the product as opposed to merely purchasing and appropriately using commercially available product, as millions of customers do each day with the vast array of products sold at health stores. DEA cannot assume that any purchase or ingestion of the product necessarily constitutes abuse; it must rely on the data that can distinguish abuse from mere consumption. The fact that kratom is purchased and consumed does not in this case establish "abuse" within the meaning of the CSA. The data do not show calls to poison control, adverse events, or threats to the public health beyond any other legitimate botanical dietary supplement. By failing to consider data that could distinguish abuse, and relying on data that is reflective of legitimate use, DEA cannot find sufficient scope, duration, or significance of abuse to ban kratom.

### **C. The Risk to Public Health, if any, Does Not Rise to the Level of an "Imminent Hazard"**

Although DEA asserts that "numerous deaths associated with kratom, which contains the main active constituents mitragynine and 7-hydroxymitragynine, have been reported indicating

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<sup>91</sup> 81 FR 59932.

<sup>92</sup> *Id.* at 59930.

<sup>93</sup> *Id.*

that this substance is a serious public health threat,” that assertion finds limited scientific support and is at odds with the conclusions in the published literature. DEA accompanied its proposed emergency scheduling order with a background information document detailing its evidence and analysis of the three factors it is required to consider before exercise of its emergency scheduling authority.<sup>94</sup> As demonstrated by the published sources referenced in that document, there has never been a published report in the literature of a death solely attributable to kratom: instead, every report published in scientific journals has involved the ingestion of kratom along with pharmaceuticals or controlled substances known to present risk of death.<sup>95</sup> A recently published, peer-reviewed article outlines well the position of the published studies: “Although death has been attributed to kratom use, there is no solid evidence that kratom was the sole contributor to an individual’s death.”<sup>96</sup> That stance reflects the published case reports: kratom has only been associated with fatalities in published studies when mixed with other pharmaceuticals or controlled substances.<sup>97</sup>

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<sup>94</sup> See U.S. Dep’t of Justice Drug Enforcement Admin., *Mitragynine and 7-Hydroxymitragynine Background Information and Evaluation of ‘Three Factor Analysis’ (Factors 4, 5, and 6) for Temporary Scheduling*, Docket No. DEA-2016-0015-0004.

<sup>95</sup> See Iain McIntyre et al., *Mitragynine ‘Kratom’ Related Fatality: A Case Report with Postmortem Concentrations*, 39 J. Anal. Toxicol. 152 (2015) (reporting the death of report of a 24-year-old man who was found to have ingested venlafaxine, diphenhydramine, mirtazapine, and ethanol in addition to mitragynine); Ritva Karinen et al., *An Accidental Poisoning with Mitragynine*, 245 Forensic Sci. Int’l e29 (2014) (reporting the death of a “middle-aged man” in Norway whose autopsy reported significant concentrations of zopiclone, citalopram, and lamotrigine in the blood as well as mitragynine); Michael F. Neerman et al., *A Drug Fatality Involving Kratom*, 58 J. Forensic Sci. S278 (2012) (reporting the postmortem analysis of a 17-year-old male that found significant concentrations of dextromethorphan, diphenhydramine, temazepam, and 7-amino-clonazepam in the blood, as well as mitragynine); Robert Kronstrand et al., *Unintentional Fatal Intoxications with Mitragynine and O-Desmethyltramadol from the Herbal Blend Krypton*, 35 J. of Anal. Toxicol. 242 (2011) (attributing 9 deaths in Sweden to Krypton, which the published study characterizes as a blend of mitragynine and O-desmethyltramadol, the main metabolite of the commercial opioid Tramadol).

<sup>96</sup> Marcus L. Warner et al., *The Pharmacology and Toxicology of Kratom: From Traditional Herb to Drug of Abuse*, 130 Int’l J. of Legal Med. 127 (2016); see also Boyer et al. at 1048 (“Although mitragynines agonize mu-opioid receptors, respiratory depression, coma, pulmonary edema and death have not, to our knowledge, been associated with human kratom ingestion.”).

<sup>97</sup> To the degree that DEA also relied on a recent publication from the Centers for Disease Control and Prevention (CDC) regarding kratom deaths, the CDC publication appears to be mistaken. In a 2016 publication, CDC wrote: “Published case reports have associated kratom exposure with psychosis, seizures, and deaths,” citing two sources. Mehruba Anwar, Royal Law, and Josh Schier, *Notes from the Field: Kratom (Mitragyna speciosa) Exposures Reported to Poison Centers – United States, 2010-2015*, 65 Morbidity and Mortality Weekly Report 748 (2016). One of the sources, a series of case reports from the Ramathibodi Poison Center in Thailand, writes “There were no deaths in either [study] group.” S. Trakulsrichai et al., *Kratom Abuse in Ramathibodi Poison Center, Thailand: A Five-year Experience*, 45 J. Psychoactive Drugs 404 (2013). The other source, a study of fourteen kratom reports made to poison centers in Texas, wrote: “There were no deaths.” Mathias B. Forrester, *Kratom Exposures Reported to Texas Poison Centers*, 32 J. Addictive Diseases 396 (2013). The CDC publication appears to have either misidentified its sources or been mistaken in its conclusions, as both sources reported no deaths from kratom. Likewise, the CDC report also stated that “deaths have been attributed to kratom in the United States,” but it cited for that proposition a single report in a newspaper article. The newspaper article reported the suicide of a 22-year-old male by self-inflicted gunshot wound. Erin Coleman, *Anguished Parents Say Exotic Drug Kratom is the Cause of Son’s Suicide*, Atlanta Journal Constitution, May 19, 2015. The article reported that the man’s parents believed that he was driven to suicide by kratom, because they found kratom in his apartment. *Id.* Although the case is tragic, it does not represent a medical judgment or an objective opinion about the involvement of kratom in the

DEA also lists summaries of unpublished autopsy or medical examiner reports in its analysis accompanying the emergency scheduling notice. DEA spokesman Melvin Patterson conceded that only “one of the deaths was directly attributable to kratom alone,”<sup>98</sup> a conclusion that is also found in DEA’s three-factor analysis. Mr. Patterson identified an autopsy report concerning a 36-year-old man living in Denver, Colorado who died following complications from an apparent seizure, as the only death attributable to kratom alone. Experts and others in the public cannot assess this conclusion as the autopsy report has not been made available to the public. We are not able to examine toxicology reports, assess medical history, or determine whether the substance that the decedent reportedly ingested contained substances other than kratom. We were, however, able to determine that the medical examiner’s report later revised its toxicology findings to state that it was “indeterminate” whether 7-hydroxymitragynine was present in the man’s bloodstream.<sup>99</sup> The Medical Examiner’s report also noted that the decedent had a “[h]istory of cardiopulmonary arrest.”<sup>100</sup> While any death associated with its use is regrettable and concerning, far more evidence is needed to qualify the substance for emergency scheduling. For example, the common botanical dietary supplement ginseng was determined to be solely responsible for a death in 2011 yet remains widely commercially available.<sup>101</sup> With only a small number of cases out of millions of users, and each case subject to multiple confounding factors, there is insufficient evidence to support a conclusion that kratom presents a public health threat because of risk of fatality.

Nor has kratom been associated with serious adverse events. Dr. Henningfield prepared a full investigation of serious adverse events associated with kratom by investigating published scientific literature, American Association of Poison Control Centers (AAPCC) Annual Reports between 1999 and 2013, and an FDA Freedom Of Information Act (FOIA) request.<sup>102</sup> His top-line conclusion was that kratom “demonstrates a very strong safety profile.”<sup>103</sup> In particular, his review found fewer than 100 serious adverse events globally, with serious adverse events primarily occurring in Southeast Asia. He also found that “[a] careful review of the case reports indicates that in most cases other causes, especially co-administered chemical substances or

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man’s death, and it is not consistent with any published study. The only other death reported by the CDC publication was the Karinen case study discussed above.

<sup>98</sup> Christopher Ingraham, *The DEA Wants to Ban Another Plant. Researchers Say the Plan is ‘Insane.’* Washington Post, Sept. 15, 2016.

<sup>99</sup> Dr. Amy Martin, Autopsy Report for [The 36-year-old Denver man], as amended March 24, 2015.

<sup>100</sup> *Id.*

<sup>101</sup> See AAPCC 2011 Annual Report of NPDS at 1123. We also note that DEA’s supporting documentation included discussion of a 45-year-old male in San Diego, California. Despite the medical examiner’s statement, we agree with DEA spokesman Melvin Patterson that this example does not represent a death solely attributable to kratom. As DEA’s case report notes, other medications were found in the home, and ethanol of unknown source was found in laboratory analysis of blood samples.

<sup>102</sup> Henningfield at 3.

<sup>103</sup> *Id.*

drugs, were likely responsible.”<sup>104</sup> As with the reports of fatal events, the reports of serious non-fatal serious adverse events nearly entirely comprise reports involving polypharmacy and confounding factors for which it is difficult to assign causation between the ingested substances. Moreover, Dr. Henningfield found that respiratory depressant effects were “substantially lower than those produced by opioids,” decreasing the risk of similar serious adverse events.

The reports of serious threats to the public health are very few in number, and all or nearly all appear to involve multiple confounding factors and indeterminate causation. At this juncture, it would be premature and contrary to sound scientific decision-making to arbitrarily assign causation to kratom or conclude that kratom constitutes an emergency threat to the public health.

#### **D. In Assessing the Need for Emergency Action. DEA Failed to Consider the Risk to Public Health and Safety from an Immediate Ban of Kratom**

The focal point of DEA’s analysis under the emergency scheduling authority is the risk to public health and safety, namely, “What if any, risk there is to the *public health*” and is immediate action necessary to “avoid an imminent hazard to the *public safety*.” In this instance, DEA failed to consider the substantial *adverse effects* that its emergency action would have on public health and safety, particularly for the substantial number of consumers who have already incorporated kratom into their self-care routines. When the product at issue has been so widely used for such a long period of time, the risk to the public health cannot be considered so narrowly as to avoid consideration of the public health impact of the banning of the product.

In the notice, DEA attempts to bolster its analysis by likening kratom to public health issues associated with opioid use and abuse. DEA notes that the “well-documented misuse and abuse of opioids and [that] their impact on communities is a public health and safety epidemic in the United States.”<sup>105</sup> Indeed, according to the CDC, from 1999 to 2014, more than 165,000 people have died in the US from overdose related to prescription opioids and HHS estimates that on an average day 78 people die from an opioid-related overdose.<sup>106</sup> What DEA seems to imply, but fails to substantiate, is that the growing use of kratom is in any way related to the opioid abuse epidemic. As discussed more fully above, there is no evidence that kratom has a potential for abuse based upon its chemistry and pharmacological characteristics and no evidence that it is actually being abused, unlike the well-documented epidemic of abuse of prescription opioids.

Quite to the contrary, the rise in the use of kratom in the United States may be, at least in part, a *response* to the opioid epidemic. Over the last 10 years or more, state and federal public health agencies have been attacking the problem of prescription opioid abuse from every

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<sup>104</sup> *Id.*

<sup>105</sup> U.S. Dep’t of Justice Drug Enforcement Admin., *Mitragynine and 7-Hydroxymitragynine Background Information and Evaluation of ‘Three Factor Analysis’ (Factors 4, 5, and 6) for Temporary Scheduling*, Docket No. DEA-2016-0015-0004, at 2.

<sup>106</sup> US Dep’t of Health and Human Servs., *The Opioid Epidemic: By the Numbers* (Jun. 2016), available at <https://www.hhs.gov/sites/default/files/Factsheet-opioids-061516.pdf>.

possible angle, including multiple efforts aimed at reducing the inappropriate use and prescribing of prescription opioid products for the treatment of pain.<sup>107</sup> As is evident from the statements of the many kratom users provided in Attachment A, many consumers are heeding the information and advice they have been hearing from public health agencies and seeking alternative methods to manage their pain with minimal or no use of prescription opioid products. These consumers have safely integrated kratom into their daily lives and have avoided the serious adverse events well-associated with the use of opioids to treat chronic pain; abuse, dependence, overdose, and death. For example:

I've lived with chronic myofascial pain since I was 19. For the last four years, I have suffered from a severe and intractable iliopsoas spasm; when it flares up, it's so bad that I've cried myself to sleep and woken up screaming in pain. I used to be on a variety of prescription medications, none of which fully helped and nearly all of which interfered with my daily functioning. Almost five years ago, I began using kratom. Within months, I had phased out almost all prescription drugs. My pain management provider has marveled at the fact that I almost never need to take narcotic pain meds. . . . Without kratom, I will almost certainly have to go back on prescription drugs."<sup>108</sup>

I am a 55 year old mother of 4 and grandmother of 6 . . . In 1995 I fell and hurt my back and had back surgery. I later, in 2006 had a large deep vein thrombosis in my left leg, from my groin to my foot. I now have permanent nerve damage and neuropathy. I was on methadone through pain management for 6 years. I tried the blocks, a neuro-stimulator, physical therapies and of course the methadone. I lived my life in a constant fog, unable to care for myself or my daughter. I stopped taking methadone in 2010 and just suffered. I spent most of my time in bed, avoiding family functions because the pain was so severe. I looked into natural pain relief and found Kratom. I have been using Kratom now for about 7 months. I function and find myself able to do more things, such as buying my own groceries due to the pain relief. I am able to think clearly and enjoy my grandkids (I missed so much time with them). Kratom gave me my life back. I love my life now. The thought of losing something natural, an herb, that is safe and effective scares me. What will my

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<sup>107</sup> See US Food & Drug Admin., *Fact Sheet – FDA Opioids Action Plan* (Sept. 13, 2016), available at <http://www.fda.gov/NewsEvents/Newsroom/FactSheets/ucm484714.htm> (including efforts to educate prescribers and patients on the safe and appropriate use of opioids and the importance of using opioids only after other pain management alternatives have been considered); US Dep't of Health and Human Servs., *Opioid Abuse in the U.S. and HHS Actions to Address Opioid-Drug Related Overdoses and Deaths* (Mar. 25, 2016), [https://aspe.hhs.gov/sites/default/files/pdf/107956/ib\\_OpioidInitiative.pdf](https://aspe.hhs.gov/sites/default/files/pdf/107956/ib_OpioidInitiative.pdf); see also Deborah Dowell, Tamara Haegerich, and Roger Chou, *CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016*, 65 CDC's Morbidity and Mortality Weekly Report 1 (2016), available at <https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm>.

<sup>108</sup> Kratom Testimonies, Attachment A, at 9

choices be then? Am I doomed to a life of severe pain, or opiates that slowly take my life away?<sup>109</sup>

While DEA bases its use of the emergency scheduling authority on the purported harm caused by the availability of kratom, DEA has failed to consider the hazard to the public health by the immediate banning of the product. An immediate ban on kratom places many consumers in the position of either living with chronic pain or turning to, or increasing the use of, the very opioid products that have caused the public health epidemic. The impact on the public health of an immediate ban on kratom would be like no other prior use of DEA's emergency scheduling authority. To fully consider the public health impact of an immediate ban of kratom, DEA must take into consideration the likely negative effect on consumer behavior and the outcomes that will follow.

#### **IV. A SIGNIFICANT BODY OF PRECEDENT DEMONSTRATES WHY DEA'S APPLICATION OF THE STATUTE IN THIS INSTANCE IS UNLAWFUL**

An imminent hazard to public safety, as that term is used in the CSA, has a very clear and precise meaning. It is specifically tied to highly dangerous substances that rapidly threaten the community based on the high abuse potential of the substance and the likelihood of criminal activity, diversion, and trafficking that amplify the rapid spread of the substance. This is evidenced by the specific factors listed in the statute that DEA is required to consider: the substance's history and current pattern of abuse; the scope, duration, and significance of abuse; and the risk there is to the public health.<sup>110</sup>

Emergency scheduling is an important law enforcement tool, and that is precisely how DEA has used this provision up until this action. A review of the precedents could not be clearer: since DEA began utilizing its emergency scheduling authority in 1985, DEA has consistently used its authority to control rapidly emerging synthetic analogs of existing controlled substances with a known high potential for abuse. DEA's historic use of its emergency scheduling authority can be fairly divided into three categories: synthetic analogs to fentanyl, a potent schedule II opioid; synthetic analogs to the "club drug" 3,4-Methylenedioxymethamphetamine (MDMA or ecstasy); and more recently, powerful synthetic cannabinoids and cathinones, substances directly associated with disturbingly bizarre adverse events and deaths.

In contrast, DEA has never exercised its emergency scheduling authority to control a natural botanical substance. It has never exercised its emergency scheduling authority to control a widely used consumer product with a long history of safe marketing and it has never exercised its emergency scheduling authority to control a substance in the absence of evidence of a high potential for abuse or an immediate threat of death or serious bodily harm. Indeed, doing so in

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<sup>109</sup> Kratom Testimonies, Attachment A, at 11.

<sup>110</sup> 21 USC 811(h)(3).

the case of kratom would be patently inconsistent with both the plain language and legislative history of the CSA.

In 1985, DEA first exercised its emergency scheduling authority to control the substance 3-methylfentanyl, a synthetic analog to fentanyl.<sup>111</sup> DEA acted swiftly to remove this new substance from the marketplace in the face of overwhelming evidence that the fentanyl analog was directly linked to a number of overdose deaths that had occurred in an eight month period preceding DEA's order.<sup>112</sup> DEA has controlled numerous additional fentanyl analogs through the emergency scheduling authority, including more recently the analogs acetyl fentanyl, butyryl fentanyl, and beta-hydroxythiofentanyl.<sup>113</sup> In its scheduling order for these substances, DEA pointed to a significant number of confirmed fatalities in the United States in which acetyl fentanyl was a contributing factor, all of which were opioid overdose related.<sup>114</sup>

Although kratom may be associated with mild stimulant effects at lower doses and more sedative effects at higher dosages,<sup>115</sup> kratom's potency and effects are not comparable to, let alone fifteen times more severe than, fentanyl or morphine. Kratom simply does not possess the same abuse potential as these substances. Further, while DEA claims that there are a small number of deaths associated with kratom, these deaths are more consistent with polypharmacologic toxicity than opioid overdose through exclusive use of kratom as there is no reference to central-nervous system or respiratory depression.<sup>116</sup>

DEA has also exercised its emergency scheduling authority to control synthetic analogs to the well-known "club drug" MDMA, or ecstasy. MDMA acts as "both a stimulant and

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<sup>111</sup> 50 FR 11690 (Mar. 25, 1985).

<sup>112</sup> *Id.* At least 31 overdose deaths associated with fentanyl analogs were reported in 1984; concentrations of the fentanyl-like substance in the body fluids of the overdose victims, in many cases, were extremely low (less than 1 ng/ml) which is consistent with the use of an extremely potent substance. *Id.*

<sup>113</sup> 80 FR 42381 (July 17, 2015) (controlling acetyl fentanyl); 81 FR 29492 (May 12, 2016) (controlling butyryl fentanyl and beta-hydroxythiofentanyl). *See also* 51 FR 4722 (Feb. 7, 1986) (controlling para-fluorofentanyl, a substance DEA estimated to be about 100 times as potent an analgesic as morphine); 50 FR 43698 (Oct. 29, 1985) (controlling thiofentanyl, acetyl-alpha-methylfentanyl, 3-methylthiofentanyl, and finding fentanyl analogs have been associated with at least 60 *narcotic overdose* deaths since January 1984).

<sup>114</sup> 80 FR 42383; Acetyl Fentanyl, Background Information and Evaluation of 'Three Factor Analysis' (Factors 4, 5 and 6) for Temporary Scheduling (April 2015).

<sup>115</sup> Henningfield at 2; Trakulsrichai et al. at 2421.

<sup>116</sup> Mitragynine and 7-Hydroxymitragynine; Background Information and Evaluation of "Three Factor Analysis" (Factors 4, 5, and 6) for Temporary Scheduling at 22-26. DEA's analysis of poison control data references a single death involving exposure to kratom, paroxetine and lamotrigine. *Id.* at 19. The FDA-approved label for paroxetine states "Since the introduction of paroxetine in the United States, 342 spontaneous cases of deliberate or accidental overdosage during paroxetine treatment have been reported worldwide (circa 1999) . . . . Of these, 48 cases were fatal and of the fatalities, 17 appeared to involve paroxetine alone." *See* Prescribing Information, Paroxetine Tablets, USP, available at: <https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=899aee24-bd00-ee0a-669d-f4f9e96ef269&type=display>. Unfortunately, DEA's notice provides little detail regarding the circumstances of these reported deaths. DEA has, therefore, further limited the opportunity for meaningful public participation in its decision making.



psychedelic, producing an energizing effect, distortions in time and perception, and enhanced enjoyment of tactile experiences.”<sup>117</sup> It is particularly attractive to adolescents and young adults “who use it to reduce inhibitions and to promote euphoria, feelings of closeness, empathy, and sexuality.”<sup>118</sup> Moreover, MDMA has well-documented neurotoxic effects.<sup>119</sup> The substance is reported to “destroy serotonergic nerve terminals and, in some cases, nerve cells in the brains of laboratory animals.”<sup>120</sup> DEA first scheduled an MDMA analog in 1987, when it temporarily placed N-ethyl MDA and N-hydroxy MDA in schedule I.<sup>121</sup> Among other evidence DEA found that both substances presented the same neurotoxicity concerns as MDMA.<sup>122</sup> Further, there were reported incidents of emergency room admission for reasons ranging from “bizarre behavior” to loss of consciousness, and deaths associated with N-ethyl MDA.<sup>123</sup>

Kratom does not possess the same or similar neurotoxicity concerns as MDMA or its synthetic analogs, nor has DEA cited evidence that kratom is particularly attractive to or likely to be abused by adolescents or young adults. DEA’s three-factor analysis in support of its emergency scheduling of kratom relies on data from the Texas Poison Center Network and National Poison Data System to show “exposures reported involved mostly young adults.”<sup>124</sup> However, if kratom was a drug of abuse among young adults, data from the Monitoring the Future survey and the National Survey on Drug Use and Health, which DEA typically considers in drug scheduling matters, would provide more clarity on any abuse among young adults. DEA’s discussion and consideration of data from these sources is conspicuously absent here.

DEA has more recently exercised its emergency scheduling authority over synthetic cannabinoids and cathinones. These substances rapidly emerged in the illicit marketplace in 2011 and have since been linked to disturbing, and in some instances bizarre, adverse events and deaths.<sup>125</sup> Synthetic cathinones and cannabinoids have purported psychotropic effects when smoked or ingested.<sup>126</sup> The adverse health effects associated with synthetic cannabinoids include

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<sup>117</sup> DEA, Drug Fact Sheet, Ecstasy or MDMA, available at: [https://www.dea.gov/druginfo/drug\\_data\\_sheets/Ecstasy.pdf](https://www.dea.gov/druginfo/drug_data_sheets/Ecstasy.pdf).

<sup>118</sup> *Id.*

<sup>119</sup> 52 FR 30176 (Aug. 13, 1987).

<sup>120</sup> *Id.*

<sup>121</sup> *Id.* The chemical description of these substances are “3,4-methylenedioxy-n-ethylamphetamine” and “N-hydroxy-3,4-methylenedioxyamphetamine,” respectively. *Id.* at 30175.

<sup>122</sup> *Id.* at 30176; *See also* 58 FR 13533 (Mar. 12, 1993) (controlling alpha-ethyltryptamine upon finding that recent scientific data also suggest that this substance may produce neurotoxicity similar to the neurotoxic effects produced by MDMA and PCA (para-chloroamphetamine)).

<sup>123</sup> 52 FR 30176.

<sup>124</sup> Mitragynine and 7-Hydroxymitragynine; Background Information and Evaluation of “Three Factor Analysis” (Factors 4, 5, and 6) for Temporary Scheduling at 11.

<sup>125</sup> *See e.g.*, 76 FR 11076 (Mar. 11, 2011) (“The emergence of these five synthetic cannabinoids represents a recent phenomenon in the U.S. designer drug market.”).

<sup>126</sup> *See id.* Clinical case reports indicate that synthetic cathinones produce a number of stimulant-like adverse effects such as palpitation, seizure, vomiting, sweating, headache, discoloration of the skin, hypertension, and hyper-

agitation, anxiety, nausea, vomiting, tachycardia, elevated blood pressure, tremor, seizures, hallucinations, paranoid behavior, and nonresponsiveness.<sup>127</sup>

In 2014, DEA emergency scheduled a number of synthetic cannabinoids, including ADB-PINACA, based on law enforcement reports that 22 persons ranging in age from 16 to 57 presented to emergency departments with severe adverse reactions after consuming a synthetic product called “Crazy Clown.”<sup>128</sup> Adverse effects included the inability to stand, foaming at the mouth, violence towards police and paramedics and memory lapse.<sup>129</sup> The substance responsible for these effects was later identified by as ADB-PINACA.<sup>130</sup> In early September 2013, 221 patients presented to emergency departments in Colorado after having adverse reactions to a synthetic product labeled as “Black Mamba.”<sup>131</sup> Adverse effects included having no gag reflex, inability to breathe on their own, hallucinations and psychotic episodes as described by nurses and attending physicians.<sup>132</sup> The substance in the product consumed was identified as ADB-PINACA.<sup>133</sup>

In February 2016, DEA emergency scheduled the synthetic cannabinoid, MAB CHMINACA or ADB-CHMINACA in schedule I.<sup>134</sup> DEA based its order on a finding that state

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reflexia. 76 FR 65371, 65373 (Oct. 21, 2011). Adverse effects associated with consumption of these drugs as reported by abusers include nose-bleeds, bruxism (teeth grinding), paranoia, hot flashes, dilated pupils, blurred vision, dry mouth/thirst, palpitations, muscular tension in the jaw and limbs, headache, agitation, anxiety, tremor, and fever or sweating. *Id.* Importantly, numerous individuals have presented at emergency departments in response to exposure incidents and several cases of acute toxicity have been reported due to the ingestion of the precise synthetic cathinones DEA has controlled through its emergency scheduling orders. *Id.* (controlling mephedrone, methylone, or MDPV). In addition, case reports have shown that the abuse of synthetic cathinones can lead to psychological dependence like that reported for other stimulant drugs. *Id.* According to clinical case reports, investigative toxicological reports, and autopsy reports, the precise synthetic cathinones DEA has scheduled have been implicated in drug induced overdose deaths. *Id.*

<sup>127</sup> 76 FR 11077. DEA has also emergency scheduled other substances that mimic the effects of schedule I hallucinogens, to an alarming extent, or are marketed as such substances yet pose significant safety risks. *See* 59 FR 671 (Jan. 6, 1994) (controlling 4-Bromo-2,5-Dimethoxyphenethylamine upon a finding that “Higher doses have been reported to produce intense and frightening hallucinations”); 68 FR 16427 (Apr. 4, 2003) (controlling AMT and 5-MeO-DIPT because they share substantial chemical and pharmacological similarities with other schedule I tryptamine-based hallucinogens, and tryptamine is known to produce convulsions and death in animals); 78 FR 68716 (Nov. 15, 2013) (controlling three synthetic phenethylamines that were often purported to be schedule I hallucinogens like lysergic acid diethylamide (LSD), and reports documented that the abuse of these substances can cause severe toxic reactions, including death). To the extent kratom has been associated with any reported incidents of hallucinations, DEA has not alleged such rise to the level of “severe” or “frightening.” Further, DEA has not proffered any evidence to suggest kratom poses similar hazard as synthetic phenethylamines.

<sup>128</sup> 79 FR 7577 (Feb. 10, 2014).

<sup>129</sup> *Id.*

<sup>130</sup> *Id.*

<sup>131</sup> *Id.*

<sup>132</sup> *Id.*

<sup>133</sup> *Id.*

<sup>134</sup> 81 FR 6171 (Feb. 5, 2016).

public health entities reported over 2,000 overdoses and at least 33 deaths across at least 11 states attributed to synthetic cannabinoids.<sup>135</sup> Moreover, DEA recognized a number of these events were caused by ingestion of the specific synthetic cannabinoid at issue.<sup>136</sup>

Likewise, in January 2015, DEA emergency scheduled the synthetic cannabinoids, AB-CHMINACA and AB-PINACA.<sup>137</sup> DEA found numerous deaths and serious adverse events directly associated with these substances including two deaths involving AB-PINACA, and one death where “the cause of death as determined by the medical examiner was toxic effects of synthetic cannabinoids: AB-CHMINACA.”<sup>138</sup> In a two-month period over 29 individuals in Gainesville, Florida, presented at local emergency departments while experiencing seizures and comas following ingestion of a synthetic cannabinoid, and laboratory analysis conducted on biological samples from 13 of the patients identified AB-CHMINACA as the drug responsible for these significant adverse effects.<sup>139</sup>

DEA’s exercise of its emergency scheduling authority outside of the three categories discussed above is also inconsistent with its use to control kratom. Specifically, in 1985, DEA exercised its emergency scheduling authority to control a substance, MPPP, which was sold on the street as “synthetic heroin.”<sup>140</sup> DEA found that patients were injecting the substance intravenously and later hospitalized with Parkinsonian symptoms.<sup>141</sup> Intravenous use of opioids increases the risk of the spread of communicable disease, including HIV/AIDs and hepatitis.<sup>142</sup> Here, DEA does not assert that individuals use kratom intravenously, likely because, they simply do not.

Similarly, DEA’s emergency scheduling of analogs of the schedule II substances amphetamine and methamphetamine serves as an example as to why emergency scheduling is inappropriate when applied to kratom.<sup>143</sup> It is well known that the illicit use of

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<sup>135</sup> *Id.* at 6173.

<sup>136</sup> N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide (MAB-CHMINACA; ADB-CHMINACA), Background Information and Evaluation of ‘Three Factor Analysis’ (Factors 4, 5, and 6) for Temporary Scheduling (August 2015) at 5.

<sup>137</sup> 80 FR 5042 (Jan. 30, 2015). These substances are N-(1-AMINO-3-METHYL-1-OXOBUTAN-2-YL)-1-(CYCLOHEXYLMETHYL) 1H-INDAZOLE-3-CARBOXAMIDE and N-(1-AMINO-3-METHYL-1-OXOBUTAN-2-YL)-1-PENTYL-1H-INDAZOLE-3-CARBOXAMIDE, respectively.

<sup>138</sup> Background Information and Evaluation of ‘Three Factor Analysis’ (Factors 4, 5, and 6) for Temporary Scheduling, AB-CHMINACA and AB-PINACA (Dec. 2014).

<sup>139</sup> *Id.*

<sup>140</sup> 50 FR 28098 (July 10, 1985).

<sup>141</sup> *Id.* at 28099.

<sup>142</sup> See Centers for Disease Control and Prevention. HIV/AIDS Statistics Overview. See <http://www.cdc.gov/hiv/statistics/index.html> (finding injection of drugs such as heroin, cocaine, and methamphetamine currently accounts for about 12 percent of new AIDS cases).

<sup>143</sup> See, e.g., 52 FR 30174, 30175 (Aug. 13, 1987) (controlling 4-methylaminorex upon finding, *inter alia*, it is a potent amphetamine-like stimulant with a low margin of safety); 53 FR 29232 (Aug. 3, 1988) (controlling N,N-dimethylamphetamine based in part on its structural similarity to amphetamine and methamphetamine, and its

methamphetamine has wreaked havoc on communities.<sup>144</sup> The immediate scheduling of methamphetamine analogs, which could be used to evade current controls and foster yet more destructive, criminal conduct, was absolutely essential. DEA asserts, but has not presented any credible evidence, that kratom possesses a high abuse potential, or that kratom – which is already widely available – has *actually* been used in any of the ways that should lead to an emergency scheduling action.

In short, the proposal to use the emergency scheduling authority to control kratom, a botanical substance with a long history of use both inside and outside the United States, is unprecedented. Emergency scheduling is an important law enforcement tool in the face of a clear and dangerous threat to public safety. The urgency of the situation allows DEA to take action ahead of its usual open, public process. The emergency scheduling authority reflects a careful balance, in which public safety takes priority over public process. As the review of the precedents shows, it would be overstepping the agency’s boundaries to use this authority for kratom. Here, instead, the public’s interest in an open, deliberate process must be given priority, given that the public has been allowed to purchase kratom over these many years, that businesses have been allowed to develop, and that, at best, the evidence of a serious safety risk has not been substantiated and is not altogether different from the risks posed by other consumer products.

## **V. DEA’S PROPOSED CONDUCT IS UNLAWFUL AS A MATTER OF ADMINISTRATIVE AND CONSTITUTIONAL LAW**

As a matter of law, a precise and exacting standard of proof is needed before DEA may invoke the extraordinary authority allowed under section 811(h). The Administrator may not invoke the authority out of caution based on inconclusive evidence.<sup>145</sup> Rather, the Administrator must find that the emergency action is “necessary to avoid an imminent hazard to public safety.” DEA simply cannot meet that standard here.

### **A. The Emergency Scheduling of Kratom Would Violate the Administrative Procedure Act**

DEA’s proposal to schedule kratom as a schedule I substance through the emergency scheduling procedures violates the Administrative Procedure Act (APA), both substantively and procedurally. DEA’s decision is *ultra vires* and contrary to the agency’s delegated authority because it constitutes a violation of a “clear and mandatory” statutory command.<sup>146</sup> As discussed

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amphetamine-like central nervous system stimulant effects); 57 FR 18824 (May 1, 1992) (same for methcathinone); 57 FR 43399 (Sept. 21, 1992) (same for aminorex).

<sup>144</sup> See DEA, Drug Threat Assessment (2015) at 45 (finding NDTs respondents reported methamphetamine as the drug that most contributes to both violent crime (38.2 %) and property crime (33.4 %)).

<sup>145</sup> Cf. *Conner v. Buford*, 848 F.2d 1441, 1454 (9th Cir. 1988) (holding that “incomplete information . . . does not excuse” an agency’s “failure to comply with the statutory requirement”).

<sup>146</sup> *Lepre v. Dep’t of Labor*, 275 F.3d 59, 71–72 (D.C. Cir. 2001); *Dart v. United States*, 848 F.2d 217, 231 (D.C. Cir. 1988).

above, DEA cannot meet the “imminent hazard to public safety” requirement for kratom based on the limited scope of evidence DEA is required to consider: the history and current pattern of abuse; the scope, duration, and significance of abuse; and the risk to the public health. DEA’s effort to stretch the reach of the emergency scheduling statute to a substance that has been used world-wide for centuries and by United States consumers for a period of decades<sup>147</sup> is simply not in keeping with the requirements imposed by Congress and not supported by the facts before the agency. As such, the agency violates its statutory mandate and is acting *ultra vires*.

Even a concerned and responsible regulator acting out of caution could not base an emergency scheduling decision on the facts and record presented here. The emergency scheduling process is only available where DEA can demonstrate that it is “*necessary* to avoid an imminent hazard to public safety.”<sup>148</sup> DEA cannot meet that standard here, and its conduct therefore is *ultra vires*.

For the same reasons, DEA’s proposed conduct also would be procedurally defective. The procedural shortcuts created by Congress for the emergency scheduling of new and dangerous substances simply are not appropriate for DEA to use in banning substances that have been on the market for years and that do not pose an “imminent hazard to public safety.” By shoehorning its efforts to ban kratom into the inapplicable (and extremely abbreviated) emergency scheduling process, DEA has sidestepped important procedural protections that otherwise would have been available under the standard scheduling rulemaking process – protections that most certainly would have changed the outcome of DEA’s decision. These include notice and comment rulemaking, Executive Orders (EOs) 12866 and 13563 and the Data Quality Act. For both substantive and procedural reasons, then, DEA’s scheduling of kratom in the proposed manner would violate the APA.

## **B. The Emergency Scheduling of Kratom Would Violate the Due Process Clause**

If implemented as proposed, DEA’s proposed emergency scheduling order for kratom also would raise serious constitutional questions. First, if the scheduling order takes effect without an opportunity for interested parties to provide comments and participate in a *meaningful* hearing, the scheduling order will violate procedural due process requirements. “An elementary and fundamental requirement of due process in any proceeding which is to be accorded finality is notice reasonably calculated, under all the circumstances, to apprise interested parties of the pendency of the action and afford them an opportunity to present their objections.”<sup>149</sup> Here, DEA is criminalizing a substance that has been used by millions of Americans for many years, yet providing only a retrospective opportunity to object. As such, the proposed scheduling order would lack fundamental fairness because it would deprive interested parties of their property

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<sup>147</sup> See Discussion in Section III.A.1.

<sup>148</sup> See also *U.S. v. Reece*, 956 F. Supp. 2d 736, 745 (W.D. La.2013) (procedures in section 811(h) “can be used only for the temporary, *emergency* addition of substances to schedule 1”) (emphasis added).

<sup>149</sup> *Mullane v. Central Hanover Trust Co.*, 339 U.S. 306, 314 (1950).

rights without providing them a sufficient opportunity to be heard.<sup>150</sup> Such “post-enforcement procedures” do not satisfy the minimum procedural safeguards guaranteed by the due process clause.<sup>151</sup>

### **C. The Emergency Scheduling of Kratom Would Constitute an Unconstitutional Taking**

In addition, the proposed scheduling order would effectuate an unconstitutional taking. “Regulation of private property may be so onerous that it violates the Takings Clause of the Fifth Amendment and requires the government to provide compensation.”<sup>152</sup> A regulatory taking occurs when “regulatory actions [] are the functional equivalent to the classic taking in which government directly appropriates private property or ousts the owner from his domain,”<sup>153</sup> as determined by an analysis of “(1) the economic impact of the action on the claimant, (2) the effects of the governmental action on the reasonable investment-backed expectations of the claimant, and (3) the character of the governmental action.”<sup>154</sup>

In this case, all three factors demonstrate that the proposed scheduling order would, if implemented, constitute a regulatory taking. First, the scheduling order would immediately impact manufacturers of products containing kratom, harming their businesses overnight. Consumers currently in possession of any product containing kratom similarly would have to disown their property interests.<sup>155</sup> Second, businesses and consumers have reasonably assumed investment-backed expectations about kratom, as the substance has been on the market in the United States for years. Moreover, the proposed scheduling order is “more than an extension of comparable regulations” because DEA has never before regulated kratom.<sup>156</sup> Third, the character of the governmental action evidences a taking; as noted above, DEA has not demonstrated that it has any reasonable scientific or medical interest in “protecting” the public against kratom. Accordingly, in the absence of just compensation to those in possession of

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<sup>150</sup> See *Mingo Logan Coal Co. v. Environ. Protection Agency*, No. 14-5305, 2016 WL 3902663, at \*20 (D.C. Cir. July 19, 2016) (asserting that an agency’s disruption of settled expectations “impos[es] a significant cost on regulated parties and contraven[es] basic notions of due process and fundamental fairness).

<sup>151</sup> See *Little v. City of Oakland*, No. C 99-00795 WHA, 2000 WL 1336608, at \*4 (N.D. Cal. Sept. 12, 2000) (asserting that inadequate pre-enforcement procedures give rise to a due process claim).

<sup>152</sup> *Ramsey Winch Inc. v. Henry*, 555 F.3d 1199, 1208 (10th Cir. 2009).

<sup>153</sup> *Lingle v. Chevron U.S.A. Inc.*, 544 U.S. 528 (2005),

<sup>154</sup> *Penn Cent. Transp. Co. v. City of New York*, 438 U.S. 104, 124 (1978).

<sup>155</sup> See, e.g., Denver Department of Environmental Health, *Denver Environmental Health Issues Consumer Advisory for Kratom Products* (Sept. 6, 2016) (stating that “follow[ing] DEA’s recent decision to place kratom plant into Schedule I of the Controlled Substances Act.... Kratom retailers are being ordered to hold products or return them to the distributor with immediate cessation of sales. Consumers who have purchased kratom should dispose of it in a manner that renders it unusable or return it to the retailer from which it was purchased.”).

<sup>156</sup> See *Rose Acre Farms, Inc. v. United States*, 559 F.3d 1260, 1266-67 (Fed. Cir. 2009) (finding factor weighed against government where new regulation was not an extension of existing regulations).

kratom or who have built businesses involving kratom, DEA's proposed scheduling order would constitute an unconstitutional taking.<sup>157</sup>

## **VI. THE EMERGENCY SCHEDULING OF KRATOM FAILS TO COMPLY WITH CRITICAL CONTROLS GOVERNING FEDERAL AGENCY ACTIONS**

DEA's proposed emergency scheduling of kratom bypasses important procedural and substantive safeguards put in place by Congress and the President designed to ensure that federal agencies properly evaluate their regulatory actions before proceeding. These types of safeguards were established to assure both proper consideration by the government of the impact of governmental actions on the public, and reliance by the government on accurate information when taking such actions. In an effort to promote rulemaking and agency decision making that ensures appropriate consideration of the impact of a governmental act on, for example, the economy, jobs, communities, and small businesses, Congress has passed laws and the President has issued orders that require agencies to consider and account for the benefits and costs of their rules, and to base their decisions on sound science. Notably, with the proposed emergency scheduling of kratom, DEA has avoided proper consideration of and compliance with several of these important requirements.

Had the proper procedures for rulemaking been followed, the government would have been required to consider relevant rulemaking related Executive Orders and laws governing agency data standards designed to ensure the government conducts important analyses and makes considered decisions. By using the emergency scheduling procedure, the DEA has avoided important considerations about the impact of their action and has failed the requirement that reliable data be used in decision making.

### **A. DEA Failed to Follow the Important Considerations, Oversight, and Public Involvement Required by Executive Orders 12866 and 13563**

As explained below, Executive Order 12866 and Executive Order 13563 impose substantial requirements on federal agencies to closely consider the impact of their actions on the public, to consider options that reduce regulatory burden and maintain flexibility and choice for the public, and to involve the public in their considerations. Specifically, Executive Order 12866, titled "Regulatory Planning and Review," requires that "significant regulatory actions" be submitted for review to the White House's Office of Information and Regulatory Affairs and the Office of Management and Budget (OMB).

A "significant regulatory action," is defined as any regulatory action that is likely to result in a rule that may:

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<sup>157</sup> See *Goldblatt v. Town of Hempstead, N.Y.*, 369 U.S. 590, 594 (1962) (asserting that "onerous" government regulation can constitute a taking and constitutionally require compensation).

- have an annual effect on the economy of \$100 million or more, or adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local, or tribal governments or communities;
- create a serious inconsistency or otherwise interfere with an action taken or planned by another agency;
- materially alter the budgetary impact of entitlements, grants, user fees, or loan programs or the rights and obligations of recipients thereof; or
- raise novel legal or policy issues arising out of legal mandates, the President's priorities, or the principles set forth in Executive Order 12866.

Further, after publication in the Federal Register of a significant regulatory action, the federal agency promulgating the action and OMB are required to make available to the public the documents exchanged between them during the review. Similarly, the federal agency must identify any substantive changes between the draft submitted to OMB and the published rule and must identify those changes made at the suggestion or recommendation of OMB.

Likewise, Executive Order 13563, "Improving Regulation and Regulatory Review,"<sup>158</sup> builds upon the principles in Executive Order 12866 by encouraging agencies to coordinate their regulatory activities, and to consider regulatory approaches that reduce the burden of regulation while maintaining flexibility and freedom of choice for the public. This Executive Order directs agencies to, where feasible and appropriate, seek the views of those likely to be affected by a proposed rulemaking before a notice of proposed rulemaking is issued. Importantly, it requires agencies to quantify anticipated benefits and costs of proposed rulemakings as accurately as possible using the best available techniques, and to ensure that any scientific and technological information or processes used to support their regulatory actions are objective. To the extent feasible and permitted by law, Executive Order 13563 also directs agencies to provide timely online access to the rulemaking docket for proposed and final rules, along with any relevant scientific and technical findings, and to afford the public the opportunity to comment on proposed regulations via the Internet.

Through these Executive Orders the President has required that federal agencies assess the potential costs and benefits of all significant regulatory actions before taking the action, and to allow for public involvement in the consideration of those actions. These requirements ensure that new regulations do not impose undue burdens on the economy and consumers and that the agency considering the regulation takes into account the views of those affected by the rules. As explained above, these Executive Orders direct OMB to review significant regulatory actions and assess the benefits and costs of proposed actions.<sup>159</sup> Even in emergency situations where time is limited, agencies must comply with OMB review to the extent practicable.<sup>160</sup>

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<sup>158</sup> 76 FR 3821; January 21, 2011.

<sup>159</sup> Exec. Order No. 12866 § 6(b).

<sup>160</sup> *Id.* § 6(a)(3)(D).



DEA maintains in the notice, without any explanation or analysis, that the proposed action is not a significant regulatory action pursuant to Executive Order 12866.<sup>161</sup> The Executive Order includes in the definition of a “significant regulatory action” any regulatory action that will have annual effect on the economy of \$100 million or more, adversely affect public health or safety, or adversely affect a sector of the economy or adversely affect jobs.<sup>162</sup> The emergency scheduling of kratom would have all four of these effects; therefore DEA erred in failing to conduct an analysis to assess these factors and to make that analysis public. Without conducting and providing an assessment of the impact on the economy and without the ability of the public to weigh in on any impact, the agency has abdicated important responsibilities. In addition, as discussed above, banning kratom could gravely harm public health and safety by prompting individuals to turn to dangerous substances with a known high potential for abuse. DEA must also conduct and release an analysis of how these downstream effects will impact the public health and safety. DEA is duty-bound to withdraw the notice.

### **B. The Emergency Scheduling of Kratom Is Contrary to the Standards Set Forth in the Data Quality Act**

DEA’s emergency scheduling notice also reflects a failure to meet the important standards of the Data Quality Act (DQA). Congress enacted the DQA to ensure that federal agencies use and disseminate accurate information. In passing the DQA, Congress was trying to prevent harm that can occur when the government relies on or provides inaccurate information. Under the DQA, all federal agency decision-making must be based on information that is controlled for “quality, objectivity, utility, and integrity,” especially statistical and scientific information.<sup>163</sup> The DQA requires federal agencies to issue information quality guidelines ensuring the quality, utility, objectivity and integrity of information that they disseminate and provide mechanisms for affected persons to correct such information. Pursuant to that directive, the United States Department of Justice (DOJ) has issued data integrity guidelines requiring public information published by the department and its constituent agencies be supported by data that is “accurate, reliable, and unbiased.”<sup>164</sup>

As described in Section III, DEA has based its proposed temporary scheduling order on information that is incomplete, in some cases inaccurate, and not analyzed appropriately. Notably, the agency relies on non-public emails with a number of analytical labs, and draws the conclusion without evidence that any increased positive results must be illicit abuse, as opposed to reflecting mere use of a commercially available consumer product. DEA also relies on data from poison control centers, without placing the information in the context of the broader population safely consuming kratom and without reference to the very similar data for similar

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<sup>161</sup> 81 FR 59933.

<sup>162</sup> Exec. Order No. 12,866 § 3(f), 58 FR 51735, 51738 (Oct. 4, 1993).

<sup>163</sup> Treasury and General Government Appropriations Act for Fiscal Year 2001, Pub. L. 106-554, § 515 (2001).

<sup>164</sup> U.S. Department of Justice, Information Quality Guidelines, *available at* <https://www.justice.gov/iqpr/information-quality>.

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botanical substances or other consumer products. Finally, DEA attributes a number of reported adverse events to kratom without examining the role of co-administered substances, and relies on unvalidated data from foreign sources.

The DQA and DOJ's implementing guidelines represent government's responsibility to ensure that policy and rulemaking is based on sound science and accurate information. DEA must withdraw the emergency scheduling notice as it is contrary to this fundamental requirement and DEA is unlikely to withstand a DQA challenge.

## VII. CONCLUSION

AKA shares DEA's concerns regarding the safe and appropriate use of kratom. AKA supports increased investment in research of the plant, to better establish its potential benefits and risks. However, AKA believes any decisions regarding kratom's status under the CSA must be accomplished through a transparent, science-based process with full opportunity for input from all stakeholders. Consumers who safely use kratom, the small businesses that have been involved in the kratom industry in the United States for decades, and scientists who have conducted, and who are in the process of conducting, important research on kratom, must be included in the process. AKA urges DEA to immediately withdraw the proposed emergency scheduling of kratom in favor of a more deliberate, constructive and inclusive process.

We greatly appreciate your consideration of this important matter of public health and public interest. Given the critical nature of the emergency scheduling action to AKA and its members, we urgently request a meeting with you or your senior staff. We will be available within a days' notice (or less) to accommodate schedules. Please contact us directly to put this meeting together.

Sincerely,



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Enclosures