December 1, 2016

Division of Dockets Management (DEA–442W)
Drug Enforcement Administration
Attn: DEA Federal Register Representative/ODW
8701 Morrissette Drive
Springfield, Virginia 22152

Re: Comments on Withdrawal of Notice of Intent to Temporarily Place Mitragynine and 7-Hydroxymitragynine into Schedule I [Docket No. DEA–442]

Dear Sir or Madam:

The Pew Charitable Trusts (Pew) offers these comments regarding the withdrawal of the notice of intent to temporarily place the main psychoactive agents of the plant kratom – mitragynine and 7-hydroxymtragynine – onto the list of scheduled controlled substances defined under the Controlled Substances Act.

Pew is an independent, nonpartisan research and policy organization with a longstanding focus on drug quality and safety. Pew's current efforts include initiatives to improve the safety of dietary supplements and expand access to evidence-based treatment for opioid and alcohol use disorders.

We commend the Drug Enforcement Agency (DEA) for considering public comment on the scheduling recommendation, and we respectfully submit the following remarks for your consideration.

Kratom and Opioid Withdrawal

Mitragynine and 7-hydroxymitragynine are the main psychoactive agents in the plant *Mitragyna speciosa*, also referred to as kratom. The plant, which is native to Southeast Asia, has both opioid and stimulant-like effects.[1]

Kratom, which is sometimes sold as a dietary supplement, has garnered a great deal of attention from media, policymakers, and regulators due to its public health risks. In 2014, the Food and Drug Administration (FDA) issued an import alert in response to an increase in shipments of products containing kratom, citing concerns about a lack of safety information.[2] The guidance advised that field

[1] Eduardo Cinosi, Giovanni Martinotti, Pierluigi Simonato, et al., "Following 'the Roots' of Kratom (*Mitragyna speciosa*): The Evoluation of an Enhancer from a Traditional Use to Increase Work and Productivity in Southeast Asia to a Recreational Psychoactive Drug in Western Countries," *Biomed Res Int* 2015 (2015): 1-11, doi: 10.1155/2015/968786.
[2] U.S. Food and Drug Administration. "Import Alert 54-15," February 28, 2014, http://www.accessdata.fda.gov/cms_ia/importalert_1137.html, accessed November 8, 2016; Josh Long, "Herb Kratom Faces Hurdles to Become Legal Dietary Supplement," *Natural Products Insider*, June 9, 2016, http://www.naturalproductsinsider.com/blogs/insider-law/2016/06/herb-kratom-faces-hurdles-to-become-legal-dietary.aspx, accessed November 8, 2016.

personnel may detain the products. In 2016, FDA officials in California seized more than 100 cases of products labeled as containing kratom, worth approximately $150,000.[3]

Kratom has been used in other countries to treat symptoms ranging from muscle pain to diarrhea, but it has recently found favor among those struggling with opioid dependency. [4] As the opioid crisis continues to plague the United States, policymakers, health care providers, and public interest groups increasingly understand that people struggling with opioid use disorders need access to effective treatments. There is evidence that medication-assisted treatment (MAT), which combines behavioral therapy with FDA-approved medications designed to managed symptoms and cravings, is the most effective approach to treating these diseases. Yet, while more than 21 million Americans have a substance use disorder, only about 10 percent of these individuals received any kind of treatment in 2014.[5] Some may have opted not to seek treatment, some may have been denied treatment, but some may have chosen to self-medicate or find a "natural" treatment.

When DEA published a notice of its intent to issue a temporary scheduling order for mitragynine and 7-hydroxymitragynine due to its purported high potential for abuse, kratom supporters mobilized, leading to DEA reopening the issue for public comment. This course of events illustrates the quandary of regulating dietary supplements, particularly those that may have pharmacological effects.

DEA and FDA Need Adequate Safety Information to Protect the Public's Health

The current regulatory system is not equipped for cases such as kratom. If kratom were an approved drug, it would have gone through testing for safety and effectiveness prior to being made available to patients. Because kratom can be sold as a dietary supplement, it does not require premarket review or approval by the FDA. This makes FDA's responsibility of conducting a thorough scientific and medical evaluation to support DEA's scheduling recommendation — on an expedited timeline — a difficult task. While FDA conducts the required safety review and DEA considers whether to schedule kratom, it remains on the market as a non-controlled substance.

Many consumers take kratom as dietary supplements to mitigate the symptoms of withdrawal from opioid dependence — a potentially deadly disease for which there are proven safe and effective medical therapies — not to promote general health and wellbeing. As the uncertainty regarding how to best regulate kratom illustrates, products promoted to treat serious or life-threatening illnesses may require more study than other supplements to ensure that regulators have the information that they need to protect public health. Imposing varying levels of regulatory scrutiny based on how these types of products will be used may be a reasonable option to protect the public's health. A similar risk-based regulatory approach was recently proposed for natural health products in Canada.[6]

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[3] U.S. Food and Drug Administration. "Kratom Seized in California by U.S. Marshals Service," *FDA News Release*, August 4, 2016, http://www.fda.gov/newsevents/newsroom/pressannouncements/ucm515085.htm, accessed November 8, 2016.

[4] Ibid.

[5] Beth Han et al., "Receipt of Services for Behavioral Health Problems: Results from the 2014 National Survey on Drug Use and Health," *National Survey on Drug Use and Health (NSDUH) Data Review*, September 2015, http://www.samhsa.gov/data/sites/default/files/NSDUH-DR-FRR3-2014/NSDUH-DR-FRR3-2014/NSDUH-DR-FRR3-2014.htm, accessed November 21, 2016.

[6] Health Canada. "Consulting Canadians on the Regulation of Self-Care Products in Canada," October 3, 2016, http://healthycanadians.gc.ca/health-system-systeme-sante/consultations/selfcare-autosoins/document-eng.php, accessed November 1, 2016.

Consumers Need Adequate Safety Information to Make Treatment Decisions

If kratom sold as a dietary supplement is effective for treating opioid withdrawal, consumers need instructions for use. Premarket safety information for drugs includes information about how much and how often to take the substance, as well as possible side effects and drug interactions. Conversely, if the product does not improve outcomes when used for opioid withdrawal, it should not be marketed for this purpose. Without testing and adequate instruction for use, kratom and other supplements can pose unknown risks. The Centers for Disease Control and Prevention (CDC) found that kratom abuse causes side effects ranging from mild (nausea and drowsiness) to severe (hypertension, seizures, psychosis). Additionally, there have been 15 deaths associated with kratom use between 2014 and 2016.[7]

Consumers also need to be assured of the purity of the supplements they take. In the U.S., regulators have seized kratom in various forms, including powders, tablets, and liquids with varying purity and quality levels.[8] If a supplement were spiked with a pharmaceutical ingredient or a banned substance, a person might only become aware of this if he or she experiences an adverse reaction. Alternatively, the possibility exists that a supplement labeled "kratom" or "mitragynine" might be something else entirely, with a host of unknown potential dangers.

Consumers need adequate information on effectiveness of kratom and similar products to make informed treatment decisions and have confidence that the products they are taking are safe. If kratom is being marketed to treat a disease — particularly, a potentially deadly disease such as opioid use disorder — truthful, non-misleading information must accompany that claim.[9] Consumers should not be responsible for distinguishing which claims are legal and which are not, and FDA does not have the resources to adequately police the vast supplement market.

Conclusion

As DEA considers whether or not to schedule kratom, we urge the agency to consider how it can work with FDA to improve the regulatory framework of these products to ensure that consumers have safe and effective treatments and understand how to use them.

We encourage DEA to make a determination about kratom's scheduling status in the interest of public health, and we thank the agency for its consideration of our comments.

Sincerely,

Elizabeth Jungman
Director, Public Health Programs
The Pew Charitable Trusts

Cynthia Reilly
Director, Substance Use Prevention
and Treatment Initiative
The Pew Charitable Trusts

[7] Federal Register (2016), 21 CFR Part 1308, "Schedules of Controlled Substances: Temporary Placement of Mitragynine and 7-Hydroxymitragynine into Schedule I." U.S. Department of Justice, Drug Enforcement Administration, 81 (169) (August 31, 2016), https://www.gpo.gov/fdsys/pkg/FR-2016-08-31/pdf/2016-20803.pdf.
[8] Ibid.
[9] 21 C.F.R. §101.14