July 27, 2026

Admiral Brian Christine
Assistant Secretary for Health
Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Docket No.: HHS-OASH-2026-0232
Re: Request for Information on Temporary Placement of 7-Hydroxymitragynine Above a Specified Threshold in Schedule I

Dear Admiral Christine:

My name is Jeffrey A. Singer. I am a Senior Fellow in Health Policy Studies at the Cato Institute. I am also a medical doctor specializing in general surgery and have been practicing that specialty in Phoenix, Arizona, for over 40 years. The Cato Institute is a 501(c)(3) non-partisan, non-profit, tax-exempt educational foundation dedicated to the principles of individual liberty, limited government, free markets, and peace. Cato scholars conduct independent research on a wide range of policy issues. To maintain its independence, the Cato Institute accepts no government funding. Cato receives approximately 80 percent of its funding through tax-deductible contributions from individuals. The remainder of its support comes from foundations, corporations, and the sale of books and other publications. The Cato Institute does not take positions on legislation.

I write to share my thoughts on your request for information on whether a scientifically justified dose threshold exists for scheduling 7-hydroxymitragynine (7-OH). The current peer-reviewed literature does not provide a scientific basis for answering that question. Although 7-OH has become the focus of increasing regulatory attention, researchers have published relatively little peer-reviewed research on its dose-related effects in humans. Animal studies demonstrate dose-dependent analgesia.[1] Other studies have examined abuse liability, as well as the development of tolerance and physical dependence following repeated administration.[2] However, researchers have published essentially no controlled

human dose-escalation studies evaluating how increasing doses of purified 7-OH affect analgesia, respiratory depression, sedation, euphoria, cognitive or psychomotor performance, or abuse liability. Researchers have likewise not systematically characterized how those effects vary across different dosing regimens in humans. As a result, the existing scientific literature does not provide a reliable empirical basis for selecting a scientifically justified dose threshold.

When the available evidence cannot answer the agency's central scientific question, the appropriate response is not to infer a scientifically unsupported threshold but to develop the evidence needed to answer it. The Department of Health and Human Services should therefore extend the comment period to allow additional research and analysis before adopting a dose threshold. The available epidemiologic evidence does not indicate an immediate public health emergency that would require the Department to act before researchers complete additional studies. The Centers for Disease Control and Prevention (CDC) reported 233 kratom-associated overdose deaths from 2015 to 2025. Over the same period, approximately 887,000 Americans died from drug overdoses nationwide.[3]

Moreover, nearly four out of five reported kratom-associated deaths involved multiple substances; opioids were present in nearly two-thirds of those deaths; and the agency concluded that it was not possible to determine which substance was primarily responsible for the clinical outcome or death in multiple-substance exposures.[4] Those findings underscore the difficulty of attributing serious harms to 7-OH alone and reinforce the need for a more complete scientific record before the Department establishes a dose threshold with significant legal and public health consequences.

The Department should also consider the unintended consequences of acting before the necessary evidence is available. Surveys consistently show that many kratom consumers use it to manage chronic pain, anxiety, post-traumatic stress disorder, depression, or opioid withdrawal.[5] The Drug Enforcement Administration (DEA) has likewise recognized that users report self-treating chronic pain with commercially available 7-OH products and cite pain and anxiety as key motivations for use.[6] If individuals who rely on these products lose access to regulated commercial sources before the scientific evidence is sufficient to support a scientifically justified dose threshold, the loss of access may lead some consumers to obtain them through illicit markets. Unlike products sold through legitimate commercial markets, illicit products offer no meaningful assurance of dose, purity, or freedom from contamination with other substances. The resulting increase in uncertainty could expose consumers to greater—not lesser—risk.

Extending the comment period would allow the Department to better evaluate both the direct risks of 7-OH and the potential unintended consequences of different regulatory approaches before establishing a scientifically justified dose threshold.

For these reasons, I respectfully urge the Department to extend the comment period and to defer selecting a dose threshold until additional research provides a sound scientific basis. Regulatory decisions with significant legal and public health consequences should rest on evidence sufficient to answer the agency's central scientific question, rather than on the absence of that evidence.

Respectfully submitted,

Jeffrey A. Singer, MD, FACS

Senior Fellow, Department of Health Policy Studies

Cato Institute

---

[1] Andrew C. Kruegel et al., "Synthetic and Receptor Signaling Explorations of the Mitragyna Alkaloids: Mitragynine as an Atypical Molecular Framework for Opioid Receptor Modulators," *ACS Central Science* 5, no. 6 (2019): 992–1001; and Kenjiro Matsumoto et al., "Antinociceptive Effect of 7-Hydroxymitragynine in Mice: Discovery of an Orally Active Opioid Analgesic from the Thai Medicinal Herb *Mitragyna speciosa*," *Life Sciences* 74, no. 17 (2004): 2143–2155.

[2] Scott E. Hemby et al., "Abuse Liability and Therapeutic Potential of the *Mitragyna speciosa* (Kratom) Alkaloids Mitragynine and 7-Hydroxymitragynine," *Neuropharmacology* 166 (2020): 107848; and Kenjiro Matsumoto et al., "Antinociception, Tolerance and Withdrawal Symptoms Induced by 7-Hydroxymitragynine, an Alkaloid from the Thai Medicinal Herb *Mitragyna speciosa*," *Life Sciences* 78, no. 1 (2005): 2–7.

[3] Centers for Disease Control and Prevention, Kratom Exposures Reported to United States Poison Centers—2015–2025, *Morbidity and Mortality Weekly Report* **75** (2026), (reporting 233 kratom-associated overdose deaths during 2015–2025). Centers for Disease Control and Prevention, National Center for Health Statistics, U.S. Drug Overdose Deaths, (national mortality data indicate approximately 887,000 U.S. drug overdose deaths during 2015–2025).

[4] Centers for Disease Control and Prevention, "Increases in Kratom-Related Reports to Poison Centers—National Poison Data System, United States, 2015–2025," *Morbidity and Mortality Weekly Report* 75, no. 11; 139-145 (March 26, 2026). (reporting that 184 of 233 kratom-associated overdose deaths [79%] involved multiple substances; opioids were present in 62% of those deaths; and noting that in multiple-substance exposures it was not possible to determine which substance was primarily responsible for the clinical outcome or death).

[5] Albert Garcia-Romeu, David J. Cox, Kirsten E. Smith, Kelly E. Dunn, and Roland R. Griffiths, "Kratom (Mitragyna speciosa): User Demographics, Use Patterns, and Implications for the Opioid Epidemic," *Drug and Alcohol Dependence*208 (2020): 107849.

[6] *Drug Enforcement Administration, *Schedules of Controlled Substances: Temporary Placement of 7-Hydroxymitragynine Above a Specified Threshold in Schedule I* (Factor 4: "History and Current Pattern of Abuse")**.** DEA notes that users report self-treating chronic pain with commercially available 7-hydroxymitragynine products and cite pain and anxiety as motivations for use. DEA also cites anecdotal reports that many users rely on these products for chronic pain.