Classification of Mitragynine-Related Compounds as Schedule I Controlled Substances

Section 1: Summary

The Ohio Board of Pharmacy (Board), pursuant to section 3719.45 of the Ohio Revised Code, proposes the placement of mitragynine-related compounds, which are some of the main active constituents of the plant kratom and substances synthesized from those compounds, into Schedule I.

Section 2: Background

Pursuant to section 3719.45 of the Revised Code, the Board shall, pursuant to emergency rule, add a previously unscheduled compound, mixture, preparation, or substance to Schedule I if the Board determines that the compound, mixture, preparation, or substance has no accepted medical use in treatment in this state and poses an imminent hazard to the public health, safety, or welfare.

In determining whether a previously unscheduled compound, mixture, preparation, or substance poses an imminent hazard to the public health, safety, or welfare, the Board shall consider all of the following with respect to the compound, mixture, preparation, or substance:

1. Its actual or relative potential for abuse;
2. The scope, duration, and significance of that abuse;
3. The risk it poses to the public health.

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Section 3: Evaluating Mitragynine-Related Compounds Under the 3-Factor Criteria

(1) The actual or relative potential for abuse.

With respect to its relative potential for abuse, mitragynine-related compounds are highly likely to follow the same pattern seen with bath salts. Bath salts were created by modifying cathinones—a primary active ingredient found in a plant called khat.[i] As soon as one of those modifications was identified and scheduled, a new cathinone-like compound was developed to evade the law. Bath salts became widely available online and at physical retail locations. "Because of their initial legal status, they were…presumed by users to be safe alternatives to other popularly abused stimulants."[ii] Rather than regulating bath salts, several states, including Ohio, and the federal government addressed this issue by banning all cathinone-like compounds (referred to as "substituted" or "synthetic" cathinones).[iii]

Similarly, mitragynine-related compounds are modified versions of kratom's primary active ingredient—mitragynine. According to the European Union Drug Agency, "[t]he chemical total syntheses reported for several kratom alkaloids are too complex to be used for economic production of any [of] these compounds. However, mitragynine can serve as a chemical precursor to the more potent 7-hydroxymitragynine."[iv] Products containing concentrated mitragynine-related compounds (e.g., 7-hydroxymitragynine (7-OH) and mitragynine pseudoindoxyl (MP)) are available to Ohio consumers today.[v] [vi]

Mitragynine can be isolated from kratom leaves and then synthetically transformed into 7-hydroxymitragynine and other semi-synthetic compounds. Using mitragynine as a scaffold, scientific researchers have designed novel opioids with significantly enhanced μ-opioid receptor activity. One such compound, MGM-15 (dihydro-7-hydroxy mitragynine), first described in 2014, is a highly potent semi-synthetic opioid that can be synthesized from 7-hydroxymitragynine in a single step. In September 2025, the presence of MGM-15 was confirmed in commercially available tablets.[vii]

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) notes that mitragynine and 7-OH are selective and full agonists of the μ-opioid receptor.[viii] Despite a long history of use originating from Southeast Asia, the widespread commercialization of kratom and products containing mitragynine-related compounds is a recent development. As kratom commercialization has grown, so too have the number of adverse events reported to poison control centers. From January 1 to July 31, 2025, poison control centers in the United States (US) received 1,690 reports of exposure cases involving kratom—a number that

already surpasses the total for all of 2024.[ix] Notably, adverse events associated with items that can be categorized as supplements are underreported. At least one source estimates the reporting rate for adverse events related to supplements to be approximately 2 percent.[x]

7-OH and MP are approximately 10 and 100 times more potent than mitragynine, respectively.[xi] At just 10 times the potency of mitragynine, the effects and actual abuse of 7-OH prompted Food and Drug Administration (FDA) Commissioner Dr. Martin Makary to warn that it could be the next wave of the opioid crisis.[xii] One study found that the amount of 7-OH in available products exceeded that found in naturally occurring material by up to 500%.[xiii] As with bath salts, each of the mitragynine-related compounds already available to consumers can be modified slightly to create a new drug and evade the law.

Kratom contains over 40 naturally occurring known alkaloids. One study examined the likely effects of 25 of those compounds. The study concluded that all the compounds share the most structural similarities with controlled opioid analgesics, such as morphine derivatives. Further analysis determined that 22 (including mitragynine) of the 25 compounds in kratom bind to μ-opioid receptors. The authors further noted:

> *The data from the PHASE model shows us that kratom compounds are predicted to affect the body just like opioids. Based on the scientific information in the literature and further supported by our computational modeling and the reports of its adverse effects in humans, we feel confident in calling compounds found in kratom, opioids.*[xiv]

In various preclinical studies, 7-OH has demonstrated greater potency than classical opioids. For example, 7-OH produces respiratory depression with more than 3-fold greater potency than morphine. According to the FDA, since the substance's therapeutic and psychoactive effects are mediated through the same μ-opioid receptor pathways as classical opioids, it can be considered to have opioid properties warranting similar regulatory consideration.[xv]

According to the FDA, no marketer has sought to develop a drug that includes kratom in the US.[xvi] Neither kratom nor any mitragynine-related compounds have been approved for medical use as a drug nor are they generally recognized as safe by the FDA. Kratom is illegal in 33 countries, including Malaysia where it is found naturally.[xvii] It is also banned in several states including Alabama, Arkansas, Indiana, Vermont, Rhode Island, Louisiana, and Wisconsin.[xviii] [xix] In August, Florida emergency scheduled 7-OH.[xx] In Ohio, the City of Toledo embargoed kratom products with Health Commissioner Karim Baroudi stating, "[w]hile some

may believe kratom to be a harmless herbal product, its effects can be unpredictable, and its sale is not allowed under current Ohio law."[xxi] On November 5, 2025, the Toledo City Council moved to ban the sale of mitragynine-related substances and, on the same day, the state of Kentucky moved to classify 7-OH as a Schedule I narcotic.[xxii] [xxiii] In December 2024, the Drug Enforcement Administration (DEA) referenced 7-OH when it identified kratom as a Drug and Chemical of Concern.[xxiv]

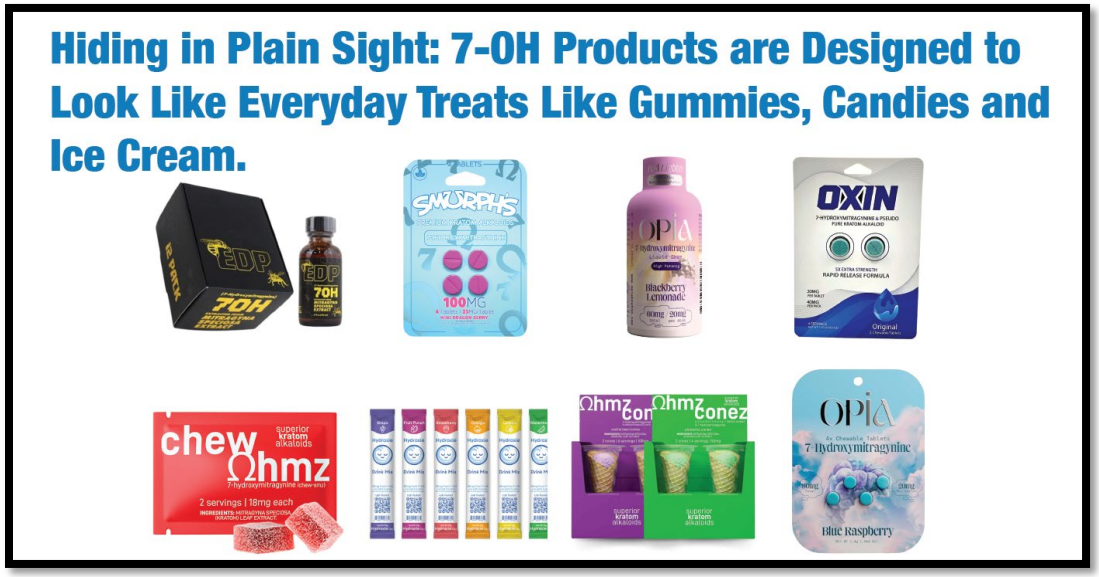
Medications approved by the FDA to treat opioid-use disorder have been used to treat individuals experiencing substance-use disorder associated with mitragynine-related compounds. For example, a case report of a male in his 40s with a history of kratom use was successfully treated with buprenorphine/naloxone, which helped alleviate his withdrawal symptoms and allowed him to abstain from kratom.[xxv] Other case examples have been cited throughout medical literature to support the use of buprenorphine/naloxone to treat kratom-use disorder.[xxvi] [xxvii] Significantly, the term kratom-use disorder is not exclusive to mitragynine, but encompasses various kratom-derived alkaloids.[xxviii]

(2) The scope, duration, and significance of abuse.

Mitragynine preparations in the US may differ significantly from traditional kratom preparations. Where isolates and extracts are widely available in the US, kratom was traditionally made from boiling fresh leaves. The impacts are notable as increased demand, including for 7-OH and MP products, has coincided with a wide variety of product preparations such as gummies, organic extracts, vapes, liquid shots, and tablets. In fact, websites stress the ease of consuming semi-synthetic products over kratom.[xxix]

On July 29, 2025, Commissioner Makary sent a letter to healthcare professionals stating that "7-OH products have exploded in popularity in recent years, with vape shops, gas stations and corner stores selling pills, gummies, candies, and even eye-catching products like ice cream cones containing 7-OH." Makary goes on to say, "increases in adverse events and related reports to poison control," raises concern "about the growth of 7-OH product sales nationwide."[xxx] Several examples of widely available products intended to look like everyday treats provided by the FDA contain multiple mitragynine-related compounds (see Figure 1).[xxxi]

Figure 1. Examples Provided by the FDA of Commercial Products Containing Mitragynine-Related Compounds



The National Drug Early Warning System (NDEWS) conducts real-time national surveillance to detect emerging drug trends. NDEWS methods include both novel methods like street reporting and web monitoring as well as traditional data sources like overdose deaths and treatment admissions. According to NDEWS, Reddit users report the following regarding mitragynine-related compounds:

> *Users describe withdrawal symptoms from concentrated alkaloid products as more severe than traditional kratom leaf, with some comparing them to pharmaceutical opioid withdrawal. Limited awareness exists about the pharmacological differences between traditional kratom and these novel derivatives, leading to unexpected overdose-like symptoms including respiratory depression concerns.*[xxxii]

The Ohio Substance Abuse Monitoring (OSAM) Network report from January 2025 found kratom use associated with opioid use, as the substance reportedly has similar effects, and kratom is reportedly advertised to help mitigate opioid withdrawal symptoms and stop opioid use. They stated: *"[a]dvertisements for kratom* [are] *on Facebook … advertised as a way to get off of opiates, certain kinds of opiates;* [Kratom] *has similar withdrawal* [symptoms as heroin]*; Kratom mimics the effects of heroin … but the POs (parole officers) are aware of it now."*[xxxiii]

A treatment provider in the Cleveland region spoke about the promoted health benefits of kratom, saying, *"[y]ou can go to the store and buy* [kratom] *now … because people look up positive things about it (health benefits). It's a pain reliever … it does give the effect of opiates or heroin…. If someone has a little pain and they think it's healthy and natural* [then they may try it]…."[xxxiv]

Reportedly, kratom is desirable because it is not always included on drug screens. Treatment providers observed: *"Kratom is still one of those things that's out there that's being abused, that's not being caught* [through drug screening]*; I spoke to our nurse practitioner, and in small doses* [kratom] *doesn't show up on the* [drug] *screen. It's because people are taking way high doses that are detectable* [on drug screens] *that are not good for you, you know, addiction wise; A lot of places don't test for it* [on drug screens]*. So, until we started testing for it, I didn't hear that much about it, but now our lab tests routinely include kratom."*[xxxv]

Internationally, the United Nations reports that the United States and Australia have reported toxicology cases with high concentration 7-OH products being involved to the UNODC Early Warning Advisory (EWA) on New Psychoactive Substances Tox-Portal. 7-hydroxymitragynine and mitragynine pseudoindoxyl are currently not controlled under the UN conventions, which are intended to establish an international legal framework for drug control.[xxxvi]

(3) The risk to the public health.

In Ohio, a growing number of deaths associated with kratom – which contains the main active constituents mitragynine and 7-hydroxymitragynine – have been reported, indicating that these compounds are a risk to public health. From 2019 to 2024, the Ohio Department of Health reported at least 202 deaths in which kratom is listed as a cause of death (see Figure 2).

Figure 2. Number of Unintentional Drug Overdose Deaths Involving Kratom (Mitragynine), 2019 - 2024[xxxvii]							
Year	Total No. Overdose Deaths	No. of Deaths with Kratom Detected in Postmortem Toxicology	% of Total Overdose Deaths with Kratom Detected in Postmortem Toxicology	No. of Deaths with Kratom Listed as a Cause of Death	% of Deaths with Kratom Detected in Postmortem Toxicology where Kratom Was Listed as a Cause of Death	No. of Deaths with Kratom Detected in Postmortem Toxicology That Were Also Positive for Other Substances	% of Deaths with Kratom Detected in Postmortem Toxicology That Were Also Positive for Other Substances
2019	3,962	19	0.5%	15	78.9%	17	89.5%
2020	4,943	34	0.7%	29	85.3%	29	85.3%
2021	5,174	49	0.9%	37	75.5%	41	83.7%
2022	4,916	47	1.0%	40	85.1%	44	93.6%
2023	4,461	52	1.2%	37	71.2%	43	82.7%
2024*	3,015	54	1.8%	44	81.5%	43	79.6%
Total	**26,471**	**255**	**0.9%**	**202**	**79.2%**	**217**	**85.1%**

**Data for 2024 is not yet complete.*

Several forensic cases of opioid-like deaths with lung congestion and high postmortem mitragynine blood concentrations with no obvious alternative causes of death have now been reported.[xxxviii] [xxxix] There is also a report of naloxone being successfully used to reverse kratom intoxication.[xl] This evidence suggests that high enough doses of kratom alkaloids may cause opioid toxicity via the usual opioid-receptor pathways implicated in conventional opioid overdoses.[xli] A recent news release from the Los Angeles County Department of Public Health reported three fatal overdoses involving high doses of 7-hydroxymitragynine and alcohol to persons who were "otherwise healthy, with no other substances identified as substantively contributing to their deaths."[xlii]

The example from Los Angeles County reinforces the dangers of respiratory depression with 7-OH. A 2025 study examining respiratory depression of morphine and 7-OH found that both induced significant respiratory depression and could be reversed using naloxone. The authors conclude that 7-OH may expose individuals to similar risks as classic opioids.[xliii]

After Utah developed a regulatory scheme to maintain over-the-counter access to kratom, overdose deaths related to kratom and treatment for kratom use disorder persisted. One emergency room physician reported patients sharing that they, "had no idea it was just like a

narcotic," and that his patients experience the same withdrawal symptoms as those withdrawing from narcotics.[xliv] The Utah State Medical Examiner reported nearly 160 kratom-related deaths over a five-year period. While most of those overdoses involved polysubstance use, the state saw almost 50% as many kratom-only deaths in the most recent 12-month reporting period as Utah had seen since 2014.[xlv] Consequently, the Utah legislature proposed to add all alkaloids from kratom and their analogs to the state's list of controlled substances in November 2025. The bill sponsor originally voted to regulate kratom in 2019 but now "sees kratom in all forms as a dangerous opioid masquerading as a supplement."[xlvi]

There are also documented cases of kratom use by expecting mothers resulting in neonatal abstinence syndrome for newborns.[xlvii] [xlviii] [xlix] These cases are particularly concerning given that the promotion of kratom products as safe alternatives to opioids may well persuade expecting mothers to consume kratom products to avoid the adverse impacts of opioids on their unborn child. The concern is compounded by the previously discussed tendency of consumers to believe that the legal status of a substance means that it is a safe alternative to a controlled substance.

Nationally, the FDA notes that the number of fatal overdose cases reported by the Drug Enforcement Administration Toxicology Testing program in which one or more of these substances were detected for 2023 to 2025 are approximately three-fold higher than for the years 2019 through 2022, coinciding with the more recent entry of mitragynine-related products in the marketplace, such as 7-OH and MP.[l]

Recent news reports also highlight the dangers of having these unregulated compounds widely available. An Akron woman reported developing "a debilitating kratom addiction" after consuming a product containing the substance thinking it was a safe, "plant-based" drink. She ended up losing her house, marriage, and half of her body weight because of her exposure and subsequent addiction to this compound. The woman reports "her addiction would have taken her life too, had she not gone to rehab in 2024."[li]

An analysis of 329 posts to Reddit online forums for kratom use between 2020 and 2022 revealed common themes of problematic use of kratom extracts leading to use disorder development and withdrawal.[lii] [liii] Furthermore, limited pre-clinical data suggest that 7-hydroxymitragynine likely confers greater misuse potential than mitragynine, again,

indicating that new, more concentrated products with higher alkaloid amounts or isolated, highly potent alkaloids may have enhanced risks to public health.[liv]

Evidence supports the position that the ingredients in mitragynine-related products available to consumers are void of robust quality control. Mitragynine-related products appear to follow the same pattern as popular natural alternatives and/or "legal highs" to controlled substances that came before it. In one study, products clearly labeled as containing the single alkaloid 7-OH all "contained at least detectable amounts of mitragynine and mitragynine pseudoindoxyl, as well as some other Kratom alkaloids."[lv]

Finally, anecdotal reports submitted to the Board highlight the dangers that kratom-related products pose to public health:

- *I am writing to urge the Board to finalize the proposed classification of 7-hydroxymitragynine (7-OH) and other kratom compounds as Schedule I controlled substances. I have personally witnessed the devastating effects of 7-OH. My husband has struggled with a severe addiction, enduring constant withdrawal symptoms and repeated relapses. The substance's easy availability in stores and online has made it nearly impossible for him to fully recover, and I have seen how accessible it puts others at risk.*[lvi]

- *Hello, I am a married wife of a kratom addict. I married my husband 7 years ago after he was clean off drugs (pills, cocaine, weed) for 8 years. He relapsed after 4 years into our marriage and has been addicted to kratom since. He was offered a sample by a gas station attendant … stated "are you looking for energy, try this". Since then he takes up to 60 capsules a day lost 25 pounds and is in a constant state of irritability, speedy, highs, and super lows withdrawling ect. He tried detox once and relapse 2 days later. He says it's so hard to quit bc it's so easy to get and cheap. This garbage is horrible and I cannot believe kids can get a hold of this junk. I am pleading for your office to understand the severity of this "supplement". My soon to be ex-husband has now transitioned to the "7oh tabs" that are more potent and also easy to get apparently sold at smoke shops and cbd stores. I know it is the choice of the individual to pick up a substance and it's their responsibility to quit, but I worry about my kids (16 and 5) in their future if they stumble upon this gas station heroine. To whatever it's worth I just wanted to share my story.*[lvii]

- *Good morning. I understand the Ohio Board of Pharmacy is considering a ban on Kratom. I am in support of this ban. I have a family member that has become addicted to Feel Free made by Botanic Tonics. It was originally marketed as a kava drink and alcohol alternative. Come to find out the company is facing many lawsuits due to its false marketing. While they now say it includes kratom, it's too late for my family. The drink is extremely addictive and very strong. I don't believe that it is pure leaf kratom, there has to be more in this drink. It has created many issues for my family and severely negatively impacted my family's life. Please consider this ban. This drink is legal opioid and available at most gas stations. This drink is very addictive and dangerous. Please seriously consider the ban on kratom and more specifically Feel Free. Also, please reference the Reddit thread quitting feelfree, you will see all the people suffering from the dangerous and addictive qualities of this drink.*[lviii]

- *My husband is a recovering opioid addict. Recently, he was introduced to kratom tablets and began taking them without telling me. When I first noticed the physical changes—his pupils shrinking and his energy levels spiking—I honestly believed he had relapsed on opioids. It was terrifying and brought back painful memories of our past struggles. He has now been taking kratom daily for months. He repeatedly tells me he plans to stop, but I can see that he cannot. He is worried about withdrawal and continues to use it despite the harm it is causing to his health and to our family. To me, this feels like we are back at square one, only with a substance that is currently unregulated and readily available. This is not the first time we have faced this danger. About a year ago, my husband was using the "blue bottle Feel Free" drinks (also containing kratom). After months of daily use, he ended up hospitalized with dangerously high liver enzyme levels and signs of serious liver damage. It took a long recovery, and now we are living through a repeat situation with kratom tablets. I know kratom is sometimes marketed as a "safe alternative" or a supplement, but my family's experience shows otherwise. For people in recovery, it is not a harmless plant—it is another addictive drug that threatens to undo years of hard work and healing.*[lix]

- *Someone very close to me began using kratom thinking it was a safe, natural way to manage stress and pain with out opiates. Over time, I watched it take over their life. They became anxious, detached, angry, and sick when they tried to stop. It broke my heart to see how something so easy to buy could cause such deep harm — not only to them, but to everyone who loves them. He would pass out while alone with our 22month*

old, he has been hospitalized with heart problems from use. We both have missed work, it has damaged our relationship, careers, children, and every aspect of our lives.[lx]

- *I'm not sure who will be reading this email or if it will really even matter but I urge you to please ban kratom and 7hydroxymitragynine. My fiancé has been addicted to this stuff almost an exact year to the day and it has torn my family apart. He has gone into close to 30k of credit card debt trying to keep up with this habit and it has cause a lot of mental distress. I know he has to take responsibility for his use and action but the first time he took a pill it was given to him FOR FREE as a sample from the clerk at the corner store. It was given to him as a "natural herbal supplement" to boost energy and help with anxiety. What was left out was that is stuff is essentially legal heroine. I am praying everyday for this to be banned and maybe when it is he will be able to actually stay sober for more than a few days at a time. This is an evil product and should 100% be taken off the shelves and made illegal.*[lxi]

Section 4: Finding of the Board

Section 3719.45 of the Revised Code authorizes the Ohio Board of Pharmacy to add a previously unscheduled compound, mixture, preparation, or substance to Schedule I if the Board determines that it has no accepted medical use in treatment in this state and poses an imminent hazard to the public health, safety, or welfare.

After a thorough review of available data, the Ohio Board of Pharmacy hereby finds that mitragynine-related compounds:

1. *Have no accepted medical use in treatment in this state; and*
2. *Pose an imminent hazard to the public health, safety, or welfare.*

Based on these findings, the Board hereby concludes that mitragynine-related compounds should be controlled in Schedule I and requests the Governor to issue an order pursuant to division (G) of section 119.03 of the Revised Code for the emergency filing of rule 4729:9-1-01.1 of the Administrative Code.

Section 5: Proposed Emergency Rule

4729:9-1-01.1 – Mitragynine-Related Compounds (NEW)

The following are classified as schedule I controlled substances:

(A) Mitragynine-related compounds, whether synthetic or naturally occurring substances contained in the plant, or in the resinous extractives of mitragyna speciosa (also known as kratom) and/or synthetic substances, derivatives, prodrugs, isomers, esters, ethers, salts and salts of isomers, esters and ethers with similar chemical structure.

Mitragynine-related compounds include, but are not limited to, the following: 7-hydroxymitragynine; mitragynine pseudoindoxyl; dihydro-7-hydroxy mitragynine; and 7-acetoxymitragynine. Mitragynine-related compounds do not include any of the following:

(1) Any dangerous drug that is the subject of an application approved by the United States food and drug administration under subsections 505(c) or (j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(c) or (j)) (December 12, 2025) for marketing as a dangerous drug;

(2) Any compound used in food consistent with either:

(a) A food additive regulation published in the United States code of federal regulations; or

(b) A “no questions response” issued by the United States food and drug administration in response to a generally recognized as safe notice.

(3) Any drug approved by the United States food and drug administration to that may be lawfully sold over the counter without a prescription in accordance with section 505G of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355h) (December 12, 2025).

(4) Mitragynine.

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