## **EXHIBIT C6**

Kratom presentation supporting materials

The kratom consumer protection act is important to pass in Arkansas. Since kratom is considered a dietary supplement, there is very little quality control taking place. This is a common issue with this market. There are thousands of stories of designer steroids, stimulants, and even opioids finding their way into pre work outs, recovery supplements, etc. The KCPA serves as a regulatory standard that must be met for all kratom products.

# What Is the Kratom Consumer Protection Act (KCPA)?

The Kratom Consumer Protection Act, or KCPA, is a bill created to protect consumers in the industry. It requires vendors to follow specific safety guidelines and good manufacturing practices, or GMP.

Since the FDA has been apprehensive about getting involved in the manufacturing and sale of kratom, the KCPA does the job of creating a space for consumers. It holds vendors accountable with a set of guidelines by the government. However, there's more to know about the Kratom Consumer Protection Act.

## The following is some of the standard text in the Kratom Consumer Protection Act:

- Prohibits the sale of kratom to minors, ages 18+ only
- Disclosing if any food items contain kratom
- Banning the sale of adulterated or contaminated kratom products
- Disallowing kratom products that are packed with or contain harmful substances that alter the strength or quality of the kratom in a way that could harm or injure the customer
- Prohibiting kratom products that may be mixed or packed with substances scheduled in the respective state
- Forbidding the sale of kratom products containing more than 2% of 7-hydroxymitragynine
- Prohibiting the sale of any products that contain synthetic kratom alkaloids or a synthetic version of any other natural compounds found in kratom
- Labeling kratom products and stating the ingredients and origin of kratom
- Disclosing the amount of mitragynine and 7-hydroxymitragynine that each product contains

The KCPA is designed to keep consumers safe and healthy while holding vendors accountable. If businesses choose not to comply with the KCPA regulations, they face hefty fines and possibly even criminal charges.

This will make sure the product is what the label claims. Knowing the concentration of mitragynine in the Kratom product is very important. Since that is the alkaloid mainly responsible for the enjoyable effects of the powder. If users do not know how much mitragynine they are taking, it can lead to unenjoyable and even dangerous effects.

There have been many examples of poorly regulated kratom products causing harm and sometimes death in the United States. The KCPA will help thwart that.

<u>J Med Toxicol.</u> 2020 Jan; 16(1): 71–74. Published online 2019 Nov 11. doi: <u>10.1007/s13181-019-00741-y</u> PMCID: PMC6942072 PMID: <u>31713176</u>

Kratom Adulterated with Phenylethylamine and Associated Intracerebral Hemorrhage: Linking Toxicologists and Public Health Officials to Identify Dangerous Adulterants

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### Heavy metals in kratom

The CDC report comes days after the Food and Drug Administration (FDA) issued a warning that products using the drug kratom aren't safe due to heavy metal contamination.

In the report, <sup>©</sup> the FDA analyzed 30 different kratom products for the presence of heavy metals. They found "significant levels of lead and nickel at concentrations that exceed safe exposure for oral daily drug intake."

The agency warns that chronic long-term exposure to nickel and lead can cause heavy metal poisoning. Symptoms may include nervous system damage, high blood pressure, and increased risk of certain cancers.

A Multiple-Serotype Outbreak of *Salmonella* Infections Linked to Kratom, United States, 2017–2018

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As I will show, millions of people use kratom in the united states. Even in states like Arkansas, where the drug is illegal, people continue using it. Keeping the drug illegal here only makes it more dangerous for the people using the drug. If we are really concerned about the safety of kratom users, we need to pass the KCPA to ensure some level of quality control so stories like these stop happening.

Meta-analysis done on studies regarding kratom withdrawal and its potential to treat opioid addiction and withdrawal.

<u>Drug Alcohol Depend Rep.</u> 2023 Jun; 7: 100142. Published online 2023 Mar 15. doi: <u>10.1016/j.dadr.2023.100142</u> PMCID: PMC1031116 PMID: <u>3739743</u>

#### Kratom withdrawal: Discussions and conclusions of a scientific expert forum $\overset{\star}{}$

<u>Jack E. Henningfield</u>,<sup>a,b,\*</sup> <u>Marek C. Chawarski</u>,<sup>c</sup> <u>Albert Garcia-Romeu</u>,<sup>b</sup> <u>Oliver Grundmann</u>,<sup>d</sup> <u>Norsyifa Harun</u>,<sup>e</sup> <u>Zurina Hassan</u>,<sup>e</sup> <u>Christopher R. McCurdy</u>,<sup>d,f,g</sup> <u>Lance R. McMahon</u>,<sup>h</sup> <u>Abhisheak Sharma</u>,<sup>f,g</sup> <u>Mohammed Shoaib</u>,<sup>i</sup> <u>Darshan Singh</u>,<sup>e</sup> <u>Kirsten E. Smith</u>,<sup>j</sup> <u>Marc T. Swogger</u>,<sup>k</sup> <u>Balasingam Vicknasingam</u>,<sup>e</sup> <u>Zachary Walsh</u>,<sup>1</sup> <u>Daniel W. Wang</u>,<sup>a</sup> and <u>Marilyn A. Huestis</u><sup>a,m</sup> Two clinical studies that systematically assessed withdrawal with the Subjective Opiate Withdrawal Scale (SOWS) and/or Clinical Opiate Withdrawal Scale (COWS) did not find evidence of withdrawal. In one, a Health Canada-approved study,198 participants (18-21 per study condition cohort) were assessed by the SOWS and COWS instruments and by adverse event monitoring for potential withdrawal signs and symptoms following daily intake of single doses of three kratom formulations at up to 29.6 mg mitragynine and following 15 consecutive daily doses (<u>Huestis et al., 2022</u>). There were no significant differences between placebo or any of the kratom dosing conditions in SOWS and COWS scores or adverse events related to withdrawal or abuse potential.

Taken together, these results suggest that withdrawal only occurs following high mitragynine intake, withdrawal signs are dissimilar and weaker than those following opioid withdrawal, and mitragynine and lyophilized kratom "tea" reduced morphine and/or heroin-related withdrawal signs (Harun et al., 2021, 2020; Hassan et al., 2021, 2020; Johari et al., 2021; Macko et al., 1972; Wilson et al., 2020; Yue et al., 2022). The differences in mitragynine and morphine withdrawal are consistent with their differing pharmacology given that mitragynine has mixed effects and mechanisms of action including partial opioid agonism, and alpha adrenergic, serotonergic and other receptor mediated effects (Behnood-Rod et al., 2020; Gutridge et al., 2020; Hassan et al., 2019; Hiranita et al., 2019; Hughes et al., 2022; Kruegel et al., 2019; Obeng et al., 2020; Patel et al., 2021; Qu et al., 2022; Suhaimi et al., 2021; Todd et al., 2020).

The various studies analyzed in this meta-analysis show clear potential to help treat opiate withdrawal and lessen self administration of these classical opioids and opiates. It has also been made very clear the withdrawal associated with quitting kratom after taking high doses daily is mild compared to these other drugs.

Behavioral studies done on kratom users has shown that regular use does not impact social or cognitive functioning.

<u>Subst Abuse Rehabil.</u> 2019; 10: 23–31. Published online 2019 Jul 1. doi: <u>10.2147/SAR.S164261</u> PMCID: PMC6612999 PMID: <u>31308789</u>

#### Current perspectives on the impact of Kratom use

Kratom use and even dependence does not impair social functioning according to several studies conducted in Malaysia.9,24 A majority of chronic Kratom users are employed, married, and live with their family and rarely present with health problems. This stands in contrast to alcohol, opioids, or amphetamine abuse that are not accepted in society.25

The use of Kratom in Southeast Asia has been documented back for at least 150 years and described both a stimulant effect for use in hard day labor when fresh leaves are chewed and an analgesic and relaxing effect if brewed into a tea. It also serves as a substitute and mitigation strategy for opium that was widely used in Malaysia and Thailand from the 1830s to the 1920s. In addition, Kratom remains in use for its antispasmodic, muscle-relaxant, and antidiarrheal effects while both its brief stimulant and analgesic effects remain a popular home remedy in Southeast Asia. P The use of Kratom is prohibited in Malaysia under Poisons Act 1952, but its use remains widely spread because the tree grows natively and tea decoctions are readily available in local communities. Thailand lifted the ban on the use, production, and possession of Kratom in 2018 for medicinal purposes. 10

Kratom users in the West are using the leaf extract and its varied formulations for a range of health reasons that primarily relate to chronic pain, mood disorders, or mitigating the withdrawal symptoms of a prescription or illicit drug dependency.<u>15</u> Although the number of Kratom users in the United States remains vague, the estimate ranges from 3 to 5 million based on survey data and membership information provided by the American Kratom Association.<u>16</u>

Millions of people use this drug yearly in the US, less than 100 deaths have been attributed to it by the CDC in the past 18 months. This drug has the potential to help people without inhibiting their ability to function properly. People who struggle with opioid or alcohol abuse can see relief through using this drug instead.

#### Pharmacology overview

Kratom has been compared to heroin, oxycodone, fentanyl, etc. many times. I will provide some basic overviews of the pharmacology of heroin, mitragynine, and buprernorphine here. Buprenorphine, also known as suboxone, has been used to treat opioid addiction and withdrawal all around the US. After reading these excerpts from pharmacological studies, it will become readily apparent why mitragynine is more like buprenorphine than heroin and fentanyl. Comparing mitragynine to heroin only misleads, it is an inaccurate comparison that leads people to forming a very skewed idea of what the drug is.

#### Open Access Article

#### Human Mitragynine and 7-Hydroxymitragynine Pharmacokinetics after Single and Multiple Daily Doses of Oral Encapsulated Dried Kratom Leaf Powder

by Marilyn A. Huestis <sup>1,\*</sup> 🗆 📴, Martin A. Brett <sup>2</sup> 🖾 😳, John Bothmer <sup>3</sup> 🗠 and Ramsey Atallah <sup>4</sup> 🗠

Kratom leaves, consumed by millions worldwide as tea or ground leaf powder, contain multiple alkaloids, with mitragynine being the most abundant and responsible for most effects. Mitragynine is a partial  $\mu$ -opioid receptor agonist and competitive antagonist at  $\kappa$ - and  $\delta$ -opioid receptors; however, unlike morphine, it does not activate the  $\beta$ -arrestin-2 respiratory depression pathway.

This shows the type of affinity mitragynine has with the mu, delta, and kappa opioid receptors. It partially agonizes the mu opioid receptors. Which means it partially activates the receptor. This is what causes the enjoyable effects of the drug. It also shows that mitragynine does not cause respiratory depression, which is the main mechanism of death by opioid overdose. This is why millions of people use the drug a year in the US and so few people die from doing so.

> Acta Pharm Hung. 2003;73(3):197-205.

### [Heroin, part III: the pharmacology of heroin]

#### Abstract

The major pharmacological effects of heroin can be traced back to some structural properties of the morphine molecule. The analgesic effects of heroin derive from the two active metabolites, 6-O-acetylmorphine and morphine, which bind specifically to the mu-opioid receptors of the central nervous system. mu-receptors also mediate other pharmacological actions of heroin i.e. respiratory depression, euphoria and physical dependence. Heroin is more potent and faster acting than

This shows that heroin *fully* agonizes the mu opioid receptor, and also activates the pathways required to cause respiratory depression.

#### **Buprenorphine**

Rachna Kumar; Omar Viswanath; Abdolreza Saadabadi.

Author Information and Affiliations

Last Update: June 8, 2024.

#### **Mechanism of Action**

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Buprenorphine is a partial agonist at the mu receptor, which means it partially activates mu-opiate receptors. The drug also acts as a weak kappa receptor antagonist and delta receptor agonist. Buprenorphine is a potent analgesic acting on the central nervous system (CNS), which possesses a distinctive quality with its partial agonism at the mu receptor. This unique characteristic imparts several notable properties, including the plateauing of its analgesic effects at higher doses, where its effects transition into an antagonistic mode. Buprenorphine exhibits ceiling effects on respiratory depression, signifying its safety superiority over methadone in the context of agonist substitution treatment for addiction.[13]

This shows that buprenorphine is also a partial agonist at the mu-opioid receptors and has a similar affinity for the delta and kappa opioid receptors. At the end of this quote it mentions a ceiling effect on respiratory depression signifying a safety superiority of methadone, as well as classical opiates. On that same note, we can look at the respiratory depression effects of mitragynine.

<u>Br J Pharmacol.</u> 2022 Jul; 179(14): 3875–3885. Published online 2022 Mar 30. doi: <u>10.1111/bph.15832</u>

PMCID: PMC9314834 PMID: <u>35297034</u>

#### The respiratory depressant effects of mitragynine are limited by its conversion to 7-OH mitragynine

Rob Hill, Andrew C. Kruegel, <sup>3</sup> Jonathan A. Javitch, <sup>4,5</sup> J. Robert Lane, <sup>1,2</sup> and Meritxell Canals, <sup>1,2</sup>

#### **Conclusions and Implications**

Both the anti-nociceptive effects and the respiratory depressant effects of mitragynine are partly due to its metabolic conversion to 7-OH mitragynine. The limiting rate of conversion of mitragynine into its active metabolite results in a built-in ceiling effect of the mitragynine-induced respiratory depression. These data suggest that such 'metabolic saturation' at high doses may underlie the improved safety profile of mitragynine as an opioid analgesic.

Again we see this pop up. Drugs that partially agonize the mu-opioid receptor are safer than drugs that fully agonize the receptor. Kratom is a safe drug, that is the point I'm making with these studies. I also hope after seeing this information you will be skeptical the next time someone compares the drug to heroin or classical opiates. Using kratom does not impact social functioning and it is not dangerous to the user. If we were to pass the kratom consumer protection act here in Arkansas it would improve the safety profile of using the drug even more. Let's work towards making the right decision for the people of Arkansas.

The Arkansas controlled substances act lists Mitragynine as an opium derivative, that is not accurate. Mitragynine and 7-OH-mitrgynine are not in any capacity related to opium. Below are pictures of the molecules side by side, it is clear that they are not related to each other at all. Mitragynine is a corynanthe-type monoterpene indole alkaloid. The kratom tree belongs to the coffee family of plants. Morphine, the primary active substance in opium is a benzylisoquinoline alkaloid. Opium poppy belongs to the papaver family. They are not related in any capacity. It should bother everyone in this

room that we have sent people to prison over a drug that isn't classified properly in our laws.

### MITRAGYNINE





Thank you, Mason Sanders.