UNITED STATES FOOD AND DRUG ADMINISTRATION

CITIZEN PETITION

Submitted Pursuant to 21 C.F.R. § 10.30

Petitioner:
FED UP! Coalition
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SUBJECT

Products Marketed as Kratom Dietary Supplements and Related Consumer Products Containing μ-Opioid Receptor Agonists

TABLE OF CONTENTS

ACTION REQUESTED

Petitioner respectfully requests prompt Agency action. FDA possesses ample existing statutory authority to address the products described herein under the Federal Food, Drug, and Cosmetic Act ("FDCA"), including authority relating to unapproved new drugs, misbranding, adulteration, and unlawful marketing. Pursuant to 21 C.F.R. § 10.30, Petitioner respectfully requests that the Food and Drug Administration ("FDA" or "the Agency"):

1. Determine that ingestible products marketed as dietary supplements, conventional foods, or other non-drug consumer products that contain kratom alkaloids, kratom-derived compounds, kratom metabolites, or semi-synthetic or synthetic analogs derived from the kratom alkaloid scaffold, where such compounds substantially activate the μ-opioid receptor, are not lawful dietary supplements and are instead subject to regulation as drugs under the Federal Food, Drug, and Cosmetic Act ("FDCA").

2. Clarify that the relevant regulatory inquiry is not limited to whether a compound occurs naturally in kratom leaf in trace quantity, but whether the finished product

delivers pharmacologically meaningful μ-opioid receptor agonist effects characteristic of an opioid drug.

3. Clarify that products containing kratom-derived metabolites, chemically transformed derivatives, concentrated alkaloid preparations, or semi-synthetic or synthetic kratom-scaffold compounds cannot evade drug regulation merely by being described as “botanical,” “kratom-derived,” “alkaloid,” “metabolite,” “extract,” or “enhanced kratom.”

4. Take appropriate enforcement action, including warning letters, seizures, injunctions, import alerts, or other lawful measures, against firms marketing such products as dietary supplements, foods, or otherwise outside the approved-drug framework.

5. Issue public guidance stating that products that, based on formulation, concentration, marketing context, or expected consumer use, deliver substantial μ-opioid receptor agonist exposure—including concentrated 7-hydroxymitragynine products, pseudoindoxyl-type products, highly concentrated mitragynine, speciociliatine, or related kratom alkaloid products, and semi-synthetic or synthetic kratom-scaffold agonists—are not lawful dietary supplements or conventional foods.

FRAMING STATEMENT

Products increasingly marketed as kratom consumer goods now include concentrated alkaloid products, metabolites sold as active ingredients, and semi-synthetic or synthetic kratom-scaffold compounds that objectively function to produce opioid-type effects. The dispositive regulatory question is functional, not botanical: whether the finished product objectively delivers substantial μ-opioid receptor agonist activity characteristic of a drug.

FDA has already recognized this principle through enforcement actions and public warnings regarding concentrated 7-hydroxymitragynine products. The same principle should be applied consistently across equivalent products regardless of nomenclature, labeling, or asserted botanical lineage.

AUTHORITIES AND REFERENCES

Authorities cited below may be supplemented or updated as appropriate. 1. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301 et seq. 2. 21 U.S.C. § 321(g)(1). 3. 21 U.S.C. § 321(ff). 4. 21 U.S.C. § 331. 5. 21 U.S.C. § 342. 6. 21 U.S.C. § 343. 7. 21 U.S.C. § 355. 8. 21 C.F.R. § 10.30. 9. U.S. Food and Drug Administration. FDA and Kratom. 10. U.S. Food and Drug Administration. FDA warning letters and enforcement actions regarding 7-hydroxymitragynine products (2025). 11. Kruegel AC, Grundmann O. Neuropharmacology.

2018. 12. Kruegel AC et al. ACS Cent Sci. 2019. 13. Kamble SH et al. ACS Pharmacol Transl Sci. 2020. 14. Váradi A et al. J Med Chem. 2016. 15. Hill K et al. Drug Alcohol Depend. 2025.

STATEMENT OF GROUNDS

I. Executive Summary

This petition concerns a rapidly evolving category of products marketed under the label of kratom or kratom-derived consumer goods that increasingly extends beyond traditional plant material into concentrated extracts, enhanced alkaloid products, metabolite-based products, and semi-synthetic or synthetic opioid-active compounds.

The common regulatory issue is not taxonomy, branding, or whether a label invokes a plant source. The relevant issue is pharmacology. Products that substantially activate the μ-opioid receptor produce effects characteristic of opioid drugs, including analgesia, abuse liability, physical dependence, withdrawal, and potentially respiratory depression.

The emergence of these products creates a serious risk that potent opioid agonists can be sold through the dietary supplement or botanical marketplace without premarket demonstration of safety and efficacy, without manufacturing and labeling controls appropriate to drugs, and without the safeguards expected for products with opioid-like pharmacology.

FDA has already made clear that products containing concentrated 7-hydroxymitragynine are being marketed illegally. The same legal and scientific logic applies more broadly to the newer generation of kratom-derived opioid agonist products.

II. The Market Has Moved Beyond Traditional Kratom Leaf Products

Historically, kratom products were primarily marketed as dried leaf material, powder, or brewed preparations. The current marketplace is materially different.

This petition does not depend on treating ordinary raw kratom leaf identically to highly engineered concentrated products. Rather, it addresses the emergence of products that deliver opioid-type pharmacologic effects through concentration, transformation, synthesis, metabolite selection, or expected consumer use.

Firms now market highly concentrated extracts, products standardized or promoted for elevated alkaloid levels, products emphasizing 7-hydroxymitragynine, products containing compounds represented as metabolites of kratom alkaloids, products containing chemically transformed kratom alkaloids, and products containing semi-synthetic derivatives derived from the kratom alkaloid scaffold.

In these products, the principal pharmacologically relevant ingredient may not be ordinary kratom leaf alkaloid content but a compound deliberately enriched, transformed, or synthesized to produce stronger opioid-like effects.

III. The Scientific Core of the Issue Is μ-Opioid Receptor Agonism

The μ-opioid receptor is the principal receptor through which classical opioids produce analgesia and many major adverse effects. Compounds that substantially activate this receptor can produce opioid-type pharmacology even when their chemical structures differ from morphine or fentanyl.

Mitragynine and certain related kratom alkaloids, including speciociliatine, warrant evaluation based on receptor activity, metabolism, dose, and finished-product exposure. Related metabolites and semi-synthetic or synthetic derivatives may raise similar concerns. 7-hydroxymitragynine is a more potent and efficacious opioid-active compound than mitragynine. Published research further demonstrates metabolic conversion pathways that can increase opioid potency and efficacy.

A finished product that objectively delivers a compound with substantial μ-opioid receptor agonism is not meaningfully a dietary supplement. It is a product delivering opioid-type drug effects.

IV. Pharmacological Continuum and Predictable Molecule Substitution

The current market should not be analyzed molecule by molecule, which allows manufacturers to stay ahead of regulation by slightly altering the active ingredient. Mitragynine, 7-hydroxymitragynine, mitragynine pseudoindoxyl, and MGM-type derivatives lie on a pharmacological continuum that includes parent alkaloids, more potent oxidative or metabolic derivatives, metabolites with distinct receptor signaling, and semi-synthetic analogs engineered to preserve or enhance opioid activity.

From a regulatory standpoint, the question should be whether the marketed product delivers a pharmacologically meaningful opioid agonist exposure, not whether the ingredient occupies one or another place in a biosynthetic or synthetic pathway.

V. Circumvention Through Concentrated Mitragynine and Related Alkaloid Products

Regulatory action limited to products containing added or isolated 7-hydroxymitragynine may be readily circumvented through reformulation toward concentrated mitragynine, speciociliatine, or related alkaloid products that deliver substantial opioid-like pharmacologic effects.

Mitragynine and related kratom alkaloids, including speciociliatine, may exhibit relevant μ-opioid receptor activity depending on compound-specific properties. Mitragynine is metabolized in humans to 7-hydroxymitragynine, a more potent agonist. Accordingly, the relevant inquiry should focus on total intended opioid exposure and receptor activation rather than the presence or absence of a single named ingredient.

Products marketed as high-potency extracts or liquid shots may present the same practical consumer-protection concerns as products containing explicitly added 7-hydroxymitragynine. So-called kratom “shots” are commonly packaged, sized, and marketed in a manner that reasonably conveys single-occasion consumption. Nominal labeling that a bottle contains multiple servings does not necessarily negate those consumer expectations. Where such products contain high quantities of alkaloids or metabolites, foreseeable real-world use may expose consumers to substantial doses inconsistent with the apparent serving representation.

VI. Metabolism Strengthens Rather Than Weakens the Case for Drug Regulation

Kratom-related pharmacology is not limited to the labeled parent compound. In vivo conversion can produce compounds with greater μ-opioid receptor activity than the administered precursor. The true pharmacological exposure of the consumer may therefore differ materially from the label name of the principal ingredient.

When a marketed product results in clinically meaningful μ-opioid receptor agonism through formulation or metabolic pathway, the product is functioning as a drug product.

VII. Pseudoindoxyl-Type and Semi-Synthetic Compounds Intensify the Concern

Pseudoindoxyl forms and semi-synthetic derivatives illustrate how far the market can move from ordinary leaf material while continuing to trade on kratom branding. Products containing such compounds are more accurately understood as pharmacologically optimized opioid-active products linked by origin or scaffold to kratom chemistry.

Where the active ingredient, as formulated or sold, delivers substantial μ-opioid receptor agonism, botanical framing does not alter the statutory analysis.

VIII. Receptor Occupancy, Potency, and Dose-Response Matter More Than Botanical Labeling

Whether a product is pharmacologically significant depends on dose, exposure, receptor affinity, efficacy, and resulting receptor occupancy. Even a compound present in trace quantity in natural leaf may become highly significant when concentrated, enriched, chemically transformed, or delivered in purified form.

Thus, the relevant question is not merely whether a molecule can be found somewhere in the plant or in a metabolic pathway. The question is whether the marketed product, as used by consumers, can produce substantial μ-opioid receptor activation.

IX. Claims of Atypical Signaling Do Not Remove These Products from Drug Regulation

Some kratom-related compounds have been described as atypical opioids or as G-protein-biased μ-opioid receptor agonists. Even if certain signaling properties were eventually shown to reduce some adverse effects, that would not eliminate dependence risk, withdrawal risk, misuse risk, or the need for drug regulation.

As μ-opioid receptor efficacy and exposure increase, opioid-typical adverse effects are expected to increase regardless of signaling profile.

X. FDA Has Already Identified the Same Basic Regulatory Problem

FDA has repeatedly stated that there are no FDA-approved kratom drug products legally marketed in the United States. FDA has further warned consumers regarding concentrated 7-hydroxymitragynine products and taken enforcement action against firms marketing such products.

These actions already reflect the core regulatory judgment that concentrated kratom-derived opioid agonists do not belong in the supplement and food marketplace. The question presented by this petition is whether FDA should apply that same judgment coherently across the broader category.

XI. Consumer Protection Concerns Are Acute

Consumers may not appreciate that a product sold as “kratom,” “extract,” “enhanced botanical,” “shot,” or “alkaloid” is functionally delivering an opioid agonist. Product composition may vary substantially, especially where chemical transformation or multiple active compounds are involved. Dependence and withdrawal may develop in individuals who believe they are using a natural supplement rather than an opioid-active product. Serving-size disclosures may also fail to reflect ordinary consumer behavior where concentrated liquid products are packaged and presented for single-session consumption despite nominal multi-serving labels.

XII. The Dietary Supplement Framework Is a Poor Fit for Opioid-Active Products

Dietary supplements are not intended as a regulatory shelter for pharmacologically potent opioid agonists. Products delivering substantial μ-opioid receptor activation are qualitatively different from ordinary supplement ingredients.

XIII. The Appropriate Regulatory Principle Is Functional and Pharmacological

FDA should expressly state that a product does not qualify for continued marketing as a dietary supplement or conventional food where, based on formulation, concentration, marketing context, or expected consumer use, the product delivers substantial μ-opioid receptor agonist effects characteristic of a drug.

Nor may manufacturers avoid regulation through nominal reformulation, relabeling, substitution of adjacent compounds, precursor strategies, or invocation of plant origin where the result is substantial μ-opioid receptor agonist exposure characteristic of a drug.

Accordingly, FDA should apply a substance-over-form approach consistent with longstanding consumer-protection principles under the FDCA.

XIV. Need for Prompt and Uniform Enforcement

Delayed or molecule-specific enforcement predictably incentivizes rapid product migration toward new analogs, metabolites, precursor-heavy formulations, concentrated extracts, or alternative alkaloid profiles (including speciociliatine-rich products) that replicate the same pharmacological effect while evading named-ingredient scrutiny. Prompt, uniform, category-wide enforcement would better protect consumers, preserve regulatory coherence, and deter gamesmanship.

XV. Requested Administrative Disposition

Petitioner respectfully requests that FDA grant this Petition, issue appropriate interpretive guidance, initiate enforcement priorities consistent with the relief requested herein, and coordinate as appropriate with other federal agencies regarding products presenting significant abuse-liability or scheduling concerns.

ENVIRONMENTAL IMPACT

Pursuant to 21 C.F.R. §§ 25.30 and 25.31, Petitioner claims a categorical exclusion from the requirement to prepare an environmental assessment because the requested action is of a type that does not individually or cumulatively have a significant effect on the human environment.

ECONOMIC IMPACT

Economic impact information will be submitted upon request of the Commissioner, pursuant to 21 C.F.R. § 10.30(b).

CERTIFICATION

The undersigned certifies that, to the best of the undersigned's knowledge and belief, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner that are unfavorable to the petition.

Respectfully submitted,

Dated: April 18, 2026

Daniel A. Busch, M.D., M.P.H.
Chair
FED UP! Coalition