Public Comment and Independent Evidence Review

7-Hydroxymitragynine and Temporary Scheduling

Evidence-Based Evaluation of the Proposed Threshold and Less-Restrictive Public-Health Alternatives

Submitted to HHS/OASH | Docket No. HHS-OASH-2026-0232 | July 2026

Submission Element	Purpose
Docket	HHS-OASH-2026-0232; Temporary Placement of 7-Hydroxymitragynine Above a Specified Threshold in Schedule I; Request for Information.
Question addressed	Whether the proposed threshold and temporary Schedule I approach are supported by the public scientific record, and whether less-restrictive emergency controls should be considered.
Position	Immediate federal regulation is warranted; the public record does not yet demonstrate that the proposed Schedule I threshold is the least harmful or uniquely necessary response.
Requested agency action	Publish the threshold derivation, distinguish hazard from exposure-adjusted risk, evaluate enforceable alternatives, and adopt transition, research, and monitoring protections.

Central thesis

Concentrated 7-OH presents a credible opioid-related hazard requiring immediate federal attention. The public record also contains substantial uncertainty regarding prevalence, exposure-adjusted risk, attributable mortality, threshold derivation, and the likely public-health effects of abrupt prohibition. HHS should therefore consider a targeted, enforceable regulatory package, transparent threshold derivation, transition protections, and active monitoring of total public-health outcomes before concluding that temporary Schedule I placement is the least harmful available response.

Contents

Executive Overview

This submission responds to HHS/OASH's Request for Information concerning the proposed threshold for temporary Schedule I placement of 7-hydroxymitragynine above a specified level. It is written for the administrative record and is intended to assist HHS, the Attorney General, and other public readers in distinguishing established evidence, regulatory inference, unresolved scientific questions, and foreseeable public-health consequences.

The submission does not argue that concentrated 7-OH products are harmless or should remain in the current retail environment. Federal notices, HHS/FDA materials, peer-reviewed pharmacology and toxicology studies, human case reports, poison-center data, FAERS reports, forensic detections, and market evidence support immediate federal attention: concentrated products have opioid pharmacology, dependence and withdrawal are documented, severe toxicity is biologically plausible and clinically reported, and the present market lacks safeguards expected for opioid-active products. The question is therefore not whether federal action is appropriate. The question is which action is most likely to reduce total harm.

- The evidence supports urgent regulation, not complacency or continued opaque retail access.
- The evidence does not presently quantify exposure-adjusted risk, a sole-agent mortality rate, or a validated toxicological breakpoint at 0.050% 7-OH or 1 milligram per article.
- Public comments and patient narratives cannot prove clinical benefit, but they do give HHS notice of foreseeable risks from abrupt removal, including withdrawal, untreated pain, counterfeit-product exposure, or return to more dangerous substances among some users.
- National overdose trends declined during the period in which commercial 7-OH became more visible. That does not prove 7-OH caused the decline; it does weigh against any simplistic national narrative that commercial 7-OH expansion coincided with rising national overdose mortality.
- A credible less-restrictive alternative must be stricter than the status quo: age limits, licensing, GMP, independent testing, dose/package caps, exact labeling, packaging controls, adverse-event reporting, sales denominators, transition support, and active enforcement.

Public-health finding

A ban may produce unintended public-health consequences that warrant careful consideration. That finding is supported as a foreseeable-risk conclusion by the public-comment record, the documented existence of dependence and withdrawal, and historical evidence that abrupt supply restrictions can alter consumer behavior. It should not be overstated as a quantified prediction absent prospective, product-verified data.

Visual Evidence Atlas

The following figures and evidence maps summarize the cited administrative and scientific record for review. They highlight the evidence boundaries most relevant to HHS's threshold determination.

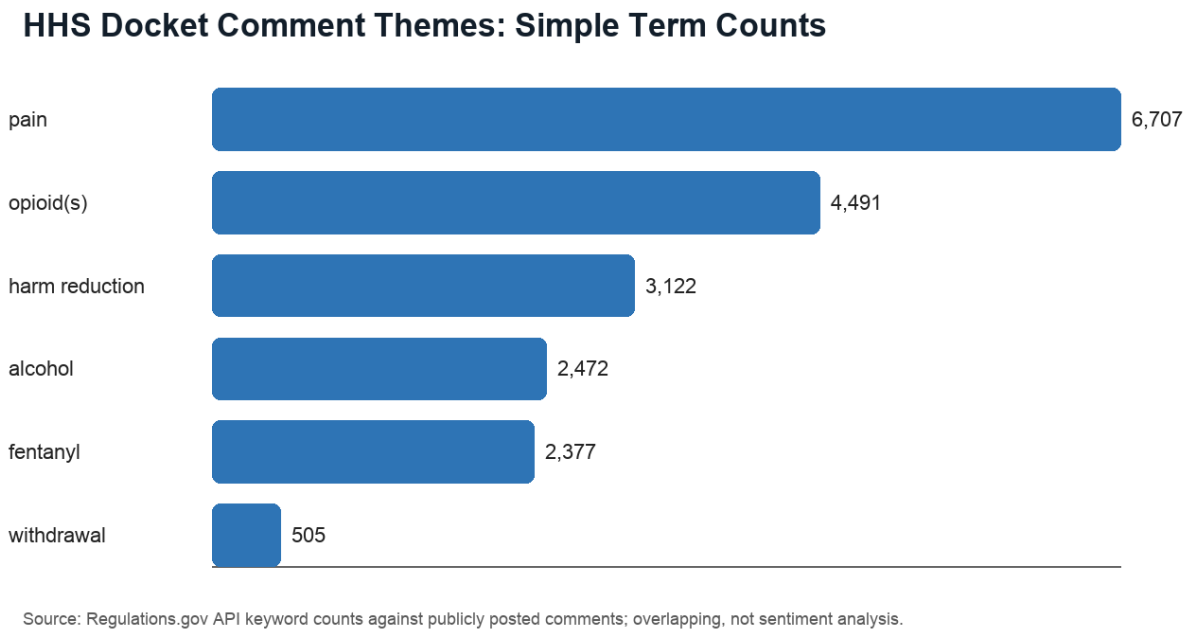

Figure 1. Public-comment term counts from Regulations.gov API searches. Counts overlap and do not represent sentiment analysis.

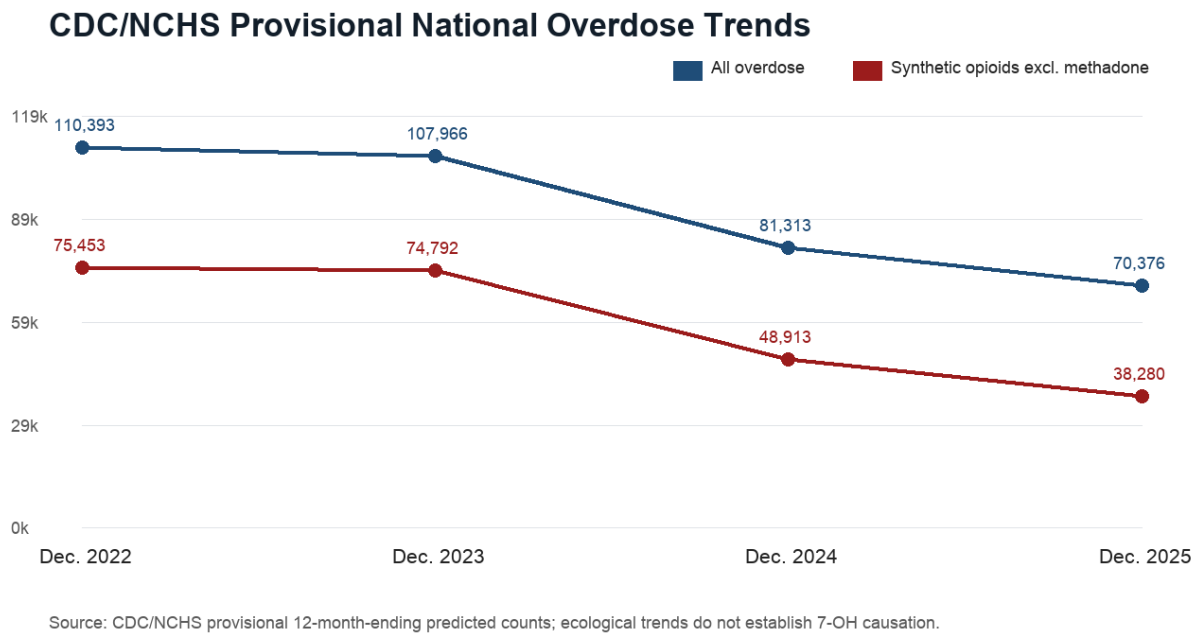

Figure 2. CDC/NCHS provisional national 12-month-ending predicted counts. These ecological data do not establish that 7-OH caused any decline.

Evidence Map: What Each Source Type Can and Cannot Support

Evidence Domain	What It Shows	What It Cannot Show	Policy Use
Pharmacology	Opioid receptor activity and opioid-like animal effects.	Human therapeutic index or population fatality rate.	Supports immediate warnings and controls.
Human cases	Dependence, withdrawal, treatment	Prevalence among all consumers.	Supports transition

	need, severe toxicity reports.		planning and clinician guidance.
Surveillance	Increasing calls, reports, detections, and safety signals.	Incidence without denominators.	Supports active monitoring and case-level audit.
Fatal detections	7-OH appears in fatal toxicology investigations.	Sole or primary causation for each death.	Requires deidentified fatality line list.
Public comments	Pain, harm-reduction, fentanyl, alcohol, and withdrawal themes.	Clinical efficacy or representativeness.	Makes substitution risk foreseeable.
Overdose trends	National overdose deaths declined after 2022.	Causal benefit from 7-OH.	Limits simplistic emergency narratives.

Scenario Matrix: Total-Harm Lens

Scenario	Potential Benefit	Potential Harm	Needed Monitoring
Status quo	No abrupt withdrawal; continued access for self-reported pain/substitution users.	Youth-accessible opioid-active products; labeling variability; continued dependence and poisoning risk.	Sales denominators, adverse events, product testing.
Strict regulated access	Reduces risky market features while preserving controlled adult access and research data.	May be slower to implement; requires enforcement capacity.	Compliance checks, adverse-event rates, purchase patterns.
Temporary Schedule I	Rapidly removes lawful retail market and sends a clear opioid-hazard signal.	Withdrawal, illicit substitution, counterfeit products, research delay, unmanaged pain.	Treatment demand, overdose, analog detections, research approvals.

Cited Federal Record Synthesis

This section synthesizes the cited Federal Register notices, HHS/OASH and FDA materials, DEA materials, peer-reviewed scientific literature, poison-center reporting, FAERS submissions, forensic toxicology reports, public comments, overdose-mortality data, and market evidence most relevant to HHS's threshold determination.

A1. Governing Questions

Record-Based Conclusions

Question	Best-Supported Answer	Confidence	Key Limitation
Does concentrated 7-OH present a credible opioid-related hazard?	Yes. Pharmacology, animal data, human cases, and surveillance reports support immediate federal concern.	High	Hazard is clearer than exposure-adjusted population risk.
Does the current record quantify national prevalence of concentrated 7-OH use?	No. The public record lacks reliable user, dose, unit, and person-year denominators.	High	Without denominators, report counts cannot become rates.
Does the record establish a sole-agent 7-OH mortality count?	No. Fatal detections are reported, but causally adjudicated line-level public data are not available.	High	Polysubstance cases may still include material 7-OH

			contribution.
Is 0.050% or 1 mg publicly validated as a toxicological breakpoint?	No. The threshold may be useful as a control threshold, but its public derivation is incomplete.	High	HHS may have nonpublic analytical rationale.
Is harm-reduction substitution plausible?	Yes, as a reported behavior and policy-relevant hypothesis.	Moderate	Not proven for concentrated 7-OH as a population-level outcome.
Is Schedule I uniquely necessary?	Not demonstrated in the public record.	Moderate	The statute may permit temporary action under uncertainty.

A2. Evidence Strength by Domain

Evidence Strength Map

Domain	Representative Sources	What Carries Weight	What Must Be Limited
Federal notices and assessments	DEA notice; HHS RFI; FDA assessment.	Regulatory rationale, proposed threshold, identified safety signals.	Do not treat agency summaries as full causal adjudication.
Receptor and animal studies	Matsumoto, Kruegel, Obeng, Hemby, respiratory-effect studies.	Intrinsic opioid hazard, reinforcement, dependence, withdrawal, respiratory depression.	Do not translate animal potency into a human fatal-dose ratio.
Human cases and treatment reports	Withdrawal cases, buprenorphine treatment reports, severe toxicity case reports.	Clinical reality of dependence, withdrawal, and serious toxicity.	Do not estimate prevalence from case reports.
Poison centers and FAERS	NPDS/MMWR, FDA spontaneous reports.	Emerging signal across multiple reporting systems.	Do not infer incidence or causation from voluntary reports.
DEA TOX and forensic reports	Fatal and nonfatal detections; broader kratom-related detections.	Detection in serious investigations and polysubstance context.	Do not say every detection was caused by 7-OH.
Market scans	Product testing, labeling, marketing, child-appealing products.	High-dose and variably labeled product category.	Do not generalize sampled products to all products without caveat.
Kratom/harm-reduction literature	Surveys, qualitative studies, EMA, pain-use studies.	Reported pain and opioid-substitution motives.	Do not transfer botanical-kratom findings automatically to concentrated 7-OH.
Overdose trend data	CDC/NCHS final and provisional overdose series.	National context and trend direction.	Do not infer 7-OH causation from ecological timing.

A3. Causation and Denominator Controls

For purposes of this submission, raw counts should be distinguished from rates, and toxicologic detection should be distinguished from causal attribution. Those distinctions are necessary for a reliable administrative record.

Numerator-to-Rate Control Table

Observed Numerator	Missing Denominator or Adjudication	Permissible Use
Poison-center calls	Number of users, units sold, doses consumed, coding changes.	Signal detection; not incidence.
FAERS reports	Exposure denominator, duplicate control, confirmed product, co-exposures.	Safety signal; not causation or rate.
DEA TOX fatal detections	Line-level cause, manner, concentrations, co-detections, product evidence.	Fatal detection evidence; not sole-agent death count.
Public comments	Representative sampling frame, sentiment coding, verification of claimed outcomes.	Foreseeable-behavior evidence; not clinical proof.
Product test purchases	National market share and sampling frame.	Market-risk illustration; not universal product characterization.

A4. Evidentiary Boundaries

- The record supports a credible opioid-related hazard, but it does not yet quantify total population risk.
- Fatality evidence should distinguish cases with 7-OH detection from cases in which 7-OH was adjudicated as the sole or primary cause.
- Potential ban effects should be treated as foreseeable risks unless prospective data support quantified predictions.
- Self-reported harm-reduction or substitution use is a public-health signal, not proof of clinical efficacy.
- The 0.050% and 1 milligram thresholds should be treated as proposed control thresholds unless HHS publishes evidence that they correspond to validated human safety boundaries.

Findings Relevant to the HHS Threshold Determination

1. Concentrated 7-OH Warrants Immediate Federal Regulation

Federal Register notices, HHS/FDA assessment materials, peer-reviewed receptor and animal studies, human case reports, poison-center analyses, FAERS submissions, forensic detections, and market evidence support a credible opioid-related hazard. Concentrated 7-OH products are not equivalent to ordinary botanical kratom: the evidence describes opioid receptor activity, reinforcement, tolerance, physical dependence, withdrawal, respiratory-depression concerns, serious poisoning reports, and a retail market that has evolved faster than clinical, toxicological, and epidemiological safeguards.

That finding supports immediate federal regulation. It does not, by itself, establish that temporary Schedule I placement is the least harmful or uniquely necessary response.

2. Hazard Identification Does Not Quantify Population Risk

The public record does not establish how many people use concentrated 7-OH, how many doses or units have been consumed, what the serious-event rate is per exposure, or how many fatal cases were caused solely or primarily by 7-OH. Raw poison-center calls, FAERS submissions, forensic detections, and case reports show that

harm exists, but they cannot become rates without a denominator and cannot become causal totals without case-level adjudication.

3. The Proposed Threshold Requires a Reproducible Basis

The proposed 0.050% and 1 milligram thresholds may be useful interim control thresholds. The public record should explain whether those values derive from botanical-background distributions, toxicological data, analytical limits, enforcement practicality, or a combination of those considerations. Unless HHS publishes evidence that the thresholds correspond to a validated human safety boundary, they should be treated as precautionary control thresholds rather than proven safe-versus-dangerous breakpoints.

4. Public Comments Identify Foreseeable Substitution and Transition Risks

The comment record is self-selected and should not be treated as a representative survey. It nevertheless gives HHS notice of foreseeable behavioral responses to abrupt removal. Large numbers of commenters describe use for pain, avoidance of fentanyl or prescription opioids, alcohol substitution, withdrawal concerns, and harm reduction. Those accounts do not prove efficacy or population-level benefit, but they are directly relevant to transition planning and total-harm analysis.

5. A Less-Restrictive Alternative Must Be Stricter Than the Status Quo

The relevant alternative is not continued opaque retail access. A credible less-restrictive approach would need enforceable age restrictions, seller licensing, GMP requirements, accredited laboratory testing, dose and package limits, plain opioid warnings, child-resistant packaging, bans on youth-oriented products, mandatory adverse-event reporting, sales-denominator reporting, recall authority, and active enforcement against adulterated or deceptively marketed products.

HHS should compare that combined emergency-control package against temporary Schedule I using total-harm criteria, including initiation, dependence, poisonings, fatalities, treatment demand, illicit substitution, counterfeit-product exposure, research access, and implementation feasibility.

Public-Health Consequences and Harm-Reduction Analysis

1. Evidentiary Use of Public Comments and Official Data

The analysis below relies on the HHS/OASH Request for Information, DEA's temporary-scheduling notice, HHS/FDA scientific assessment materials, Regulations.gov public comments, CDC/NCHS overdose mortality data, poison-center reporting, FAERS submissions, forensic toxicology reporting, peer-reviewed pharmacology and toxicology studies, human case reports, market evidence, and botanical-kratom survey literature. Established evidence, public-comment signals, plausible inference, and unsupported claims are kept separate because each category can support a different kind of agency finding.

Public comments are relevant evidence of lived experience and foreseeable behavioral responses. They are not proof of clinical efficacy, population-level safety, or population-level benefit.

Evidence Boundary

Category	How It Is Used	Examples
Established evidence	Supports direct factual conclusions when backed by federal records, peer-reviewed literature, official surveillance, or case-level evidence.	7-OH has opioid pharmacology; withdrawal and severe toxicity have been reported.

Public-comment signal	Identifies recurring themes and likely affected groups.	Pain, fentanyl avoidance, alcohol substitution, withdrawal concerns, and harm-reduction language.
Plausible inference	Supports cautious policy inference only when uncertainty is explicit.	Abrupt removal may shift some dependent or opioid-experienced consumers toward illicit opioids, counterfeit products, alcohol, or unmanaged pain.
Unsupported claim	Excluded or reframed.	7-OH caused the national overdose decline; Schedule I will inevitably cause a fentanyl surge; public comments are a representative national survey.

2. Current Docket and Comment Signal

The HHS/OASH docket is open for comments on the proposed 7-OH threshold. A recent Regulations.gov API retrieval performed for this submission returned 8,983 publicly posted comments. Because public-facing, API, and agency-internal counts may differ depending on processing status, this submission uses the conservative phrase publicly posted comments.

Public-Comment Term Counts

Search Term	Posted-Comment Matches	What It Supports	What It Does Not Support
pain	6,707	Pain management is a dominant comment theme.	Clinical efficacy for pain.
opioid/opioids	4,491	Commenters frequently frame 7-OH in relation to opioids.	Whether 7-OH lowers opioid risk in the population.
harm reduction	3,122	Many commenters use explicit harm-reduction language.	A validated harm-reduction indication.
alcohol	2,472	Some commenters discuss alcohol substitution or comparison.	That 7-OH treats alcohol-use disorder.
fentanyl	2,377	A substantial subset describes fentanyl avoidance, fear, or return risk.	That banning 7-OH will cause a quantified fentanyl increase.
withdrawal	505	Withdrawal and treatment-transition concerns are present.	Prevalence of withdrawal among all users.

Interpretation

The comment record supports a strong administrative point: HHS has notice that many affected individuals expect prohibition to change their behavior. It does not permit a claim that 90 percent of commenters are objectively pro-7-OH unless a separate, transparent sentiment analysis is performed on an exportable comment corpus.

3. Harm-Reduction and Substitution Hypothesis

The public record supports the conclusion that a ban may produce unintended public-health consequences warranting careful consideration. The evidence does not support a stronger categorical statement that a ban will

create a quantified public-health crisis. It does support treating substitution risk as plausible, historically informed, and administratively relevant.

Public comments describe several pathways: consumers using 7-OH for chronic pain after difficulty obtaining conventional care; consumers reporting avoidance of prescription opioids, fentanyl, heroin, or alcohol; physically dependent consumers fearing withdrawal; and some commenters predicting return to illicit markets if lawful access ends. These accounts cannot establish efficacy or incidence, but because they describe intended future behavior, they are relevant to policy design.

Substitution Pathways

Potential Pathway	Evidence Type	Confidence	Required Caution
Pain substitution	Regulations.gov public comments; botanical-kratom survey literature; human case reports.	Moderate that some consumers report it.	Do not infer analgesic efficacy for concentrated 7-OH.
Avoidance of fentanyl or heroin	Public comments; kratom self-treatment literature.	Moderate-low for concentrated 7-OH.	Do not infer reduced mortality without prospective data.
Alcohol substitution	Public comments.	Low-moderate as a reported behavior.	Do not infer treatment efficacy for alcohol-use disorder.
Withdrawal after removal	Human 7-OH case reports; public comments.	Moderate that dependent consumers exist.	Prevalence and severity are unknown.

Counterfeit or analog market shifts are also plausible, but that point rests on drug-policy history and analog-market experience rather than product-specific 7-OH outcome data. The analogy warrants monitoring total harm, not treating market displacement as certain.

Administrative Relevance for HHS

Thousands of public comments describe the use of 7-OH as a self-directed pain-management, opioid-substitution, alcohol-substitution, or harm-reduction strategy. These reports do not prove safety, efficacy, or population-level benefit. They do establish that abrupt removal may produce foreseeable behavioral changes, including withdrawal, return to more dangerous substances, counterfeit-product exposure, or unmanaged pain. HHS should evaluate and mitigate those risks before or alongside any temporary scheduling action.

4. National Overdose Trends

National overdose data are important but easily misused. CDC/NCHS provisional counts are 12-month-ending estimates and can differ from final annual counts. Drug-specific categories also overlap because a single death may involve multiple substances.

CDC/NCHS Provisional 12-Month-Ending National Trends

12-Month Ending	Predicted Drug Overdose Deaths	Predicted Synthetic Opioid Deaths Excl. Methadone	Interpretation
Dec. 2022	110,393	75,453	High-water period in this selected series.
Dec. 2023	107,966	74,792	Decline begins in national provisional series.
Dec. 2024	81,313	48,913	Large national decline; final annual 2024 counts differ because final data use a different reporting basis.
Dec. 2025	70,376	38,280	Continued decline in current provisional dashboard.
Feb. 2026	68,641	Not available from selected query	Early 2026 12-month-ending total remains lower than Dec. 2025.

These data support two limited points. First, they do not prove that 7-OH reduced overdose deaths. Second, they do not support a simple national narrative that increased visibility of commercial 7-OH was accompanied by a rising national overdose-death wave.

The appropriate public-health question is product-specific and exposure-adjusted: among otherwise comparable people, does verified use of concentrated 7-OH increase or decrease fatal overdose, nonfatal overdose, fentanyl exposure, alcohol use, pain and function, treatment entry, dependence, and withdrawal? The public record does not yet answer that question.

5. Drug-Policy History and Abrupt Removal Risk

Drug-policy history supports caution about measuring success solely by reduced access to a target product. The analogy is not that 7-OH scheduling will necessarily send users to fentanyl. The narrower lesson is that removing one product can change what people buy rather than eliminate why they use it.

Current federal pain and opioid guidance also warns against abrupt discontinuation in physically dependent patients. That principle does not convert 7-OH into an approved medication, but it does make withdrawal and transition planning a public-health variable.

Transition Risks and Mitigations

Foreseeable Harm	Mechanism	Mitigation
Withdrawal surge	Physically dependent consumers may lose access abruptly.	Public taper guidance, clinician alerts, poison-center guidance, low-barrier treatment referral.
Illicit substitution	Some consumers report prior fentanyl, heroin, or prescription-opioid exposure.	Naloxone distribution, treatment access, surveillance for fentanyl-related events after implementation.
Counterfeit or analog products	Demand may shift to unregulated online or illicit channels.	Laboratory surveillance for analogs, enforcement against counterfeit products, public warnings.
Unmanaged pain	Commenters describe chronic pain and limited access to conventional pain care.	Referral pathways, patient communication, non-abandonment principles, research on pain outcomes.
Research delay	Schedule I adds registration, sourcing, and handling burdens.	Expedited research registration, reference standards, grants, protocol templates.

6. Public-Health Measures for Agency Consideration

10. Publish an explicit transition plan before any order becomes effective, including withdrawal expectations, taper cautions, and guidance for clinicians unfamiliar with 7-OH dependence.
11. Coordinate low-barrier access to medications for opioid use disorder and withdrawal management.
12. Expand naloxone messaging and availability for consumers reporting opioid histories, sedative co-use, or return-to-use risk.
13. Create active surveillance indicators for poison-center calls, emergency department visits, treatment demand, seizures, counterfeit products, analog detections, fatal and nonfatal overdoses, and reports of return to fentanyl, heroin, prescription opioids, or alcohol.
14. Preserve and accelerate research access through standardized reference materials, expedited registration, and prospective studies comparing verified 7-OH, botanical kratom, MOUD, and other real-world choices.

Less-Restrictive Regulatory Framework

A less-restrictive framework must be more than voluntary self-policing. It must directly address the risk mechanisms identified by DEA, FDA, poison centers, case reports, market scans, and public comments.

Control	Purpose	Why It Matters
Age 21 and ID verification	Reduce youth initiation.	Comment record and product scans raise concerns about ordinary retail access.
Manufacturer/retailer licensing	Create accountable entities.	Current market opacity prevents traceability and recall.
Drug-like GMP and batch records	Improve consistency.	Dose variability converts consumer choice into uncontrolled exposure.
Independent ISO-accredited testing	Verify concentration, contaminants, and alkaloid profile.	A threshold cannot work without reliable measurement.
Unit, serving, and package caps	Limit high-dose exposure and anti-circumvention packaging.	Concentration alone can be evaded by larger products.
Plain opioid warnings	Communicate dependence, withdrawal, respiratory depression, and interaction risks.	Natural branding should not obscure opioid pharmacology.
Child-resistant packaging and marketing limits	Reduce accidental and youth exposure.	Candy-like or youth-oriented presentations are incompatible with opioid-active products.
Serious adverse-event reporting	Create numerator data.	Voluntary reporting cannot support incidence estimates.
Sales and total-milligrams reporting	Create denominator data.	Without denominators, agencies cannot calculate risk rates.
Transition and treatment plan	Reduce abrupt-removal harms.	Dependent users and substitution-risk groups require preparation.

Formal Public Comment

Submitted to: U.S. Department of Health and Human Services, Office of the Assistant Secretary for Health

Docket: HHS-OASH-2026-0232

Re: Temporary Placement of 7-Hydroxymitragynine Above a Specified Threshold in Schedule I; Request for Information

Commenter: Levi Matthew Beers / Co-Founder, Keystone Web Studios / Altoona, PA

Date: July 28th 2026

I. Summary

I respectfully submit this comment in response to HHS's Request for Information concerning the proposed threshold for 7-hydroxymitragynine (7-OH). I recognize that concentrated 7-OH is not equivalent to ordinary botanical kratom and that it presents genuine opioid-related risks, including reinforcement, tolerance, physical dependence, withdrawal, respiratory depression, and serious poisoning. The growing availability of high-dose products without consistent manufacturing, labeling, age controls, or post-market surveillance warrants prompt federal action. [R1-R3,R13-R22,R28-R32]

The present public record, however, does not establish the population prevalence of concentrated 7-OH use, exposure-adjusted rates of overdose or dependence, the number of deaths caused solely or primarily by 7-OH, or the comparative effectiveness of temporary Schedule I placement versus less restrictive emergency controls. HHS and FDA's own scientific assessment identifies important limitations: no controlled clinical study of isolated or purified 7-OH, no reliable prevalence estimate, difficulty distinguishing ingested 7-OH from metabolic formation after mitragynine use, frequent polysubstance exposure, and the inability of spontaneous reports to establish incidence or causation. [R3]

I therefore ask HHS to recommend a calibrated approach that protects the public immediately while preserving access to research and avoiding unsupported causal claims. At minimum, HHS should require a transparent analytical basis for the 0.050% and 1.00-milligram thresholds; distinguish concentration from absolute dose; preserve a clear botanical-material safe harbor; publish deidentified case-level mortality data; require sales and exposure denominators; and evaluate age limits, licensing, GMP, accredited testing, dose and package limits, warnings, child-resistant packaging, retail restrictions, and behind-counter or pharmacy-only access before concluding that Schedule I is the uniquely necessary response.

II. The hazard is real, but hazard is not the same as population risk

Receptor and animal studies support the conclusion that 7-OH is an opioid agonist with abuse and dependence potential. Studies report analgesic effects, morphine-like stimulus effects, reward or reinforcement, tolerance, withdrawal, and respiratory depression. The emerging human literature includes cases of high-dose frequent use, clinically meaningful withdrawal, treatment with buprenorphine or methadone, and severe opioid toxicity responsive to naloxone. These findings justify strong warnings and enforceable controls. [R15-R22,R28-R32]

Those studies establish intrinsic hazard. They do not establish how often serious outcomes occur among users, per dose, per unit sold, or per person-year of exposure. None is a controlled human study of isolated commercial 7-OH that defines a therapeutic index, chronic safety profile, interaction risk, or comparative overdose risk. A scientifically sound policy should not minimize the hazard, but it should distinguish hazard identification from risk characterization.

III. The proposed threshold requires a reproducible scientific and analytical foundation

The proposed rule uses both a concentration threshold and an absolute-amount threshold. That is directionally sensible because concentration alone can be circumvented by larger servings or containers. The public materials do not, however, explain whether 0.050% or 1.00 milligram represents a demonstrated toxicological breakpoint, a botanical-background distribution, an analytical limit, an enforcement compromise, or a combination of those considerations. HHS should make that derivation explicit. [R1-R3,R23-R26]

A final threshold framework should define at least the following: “botanical material,” “processed,” “synthetic,” “semi-synthetic,” “article,” “unit,” “serving,” and “package”; whether percentages are measured on a dry-weight, as-sold, or reconstituted basis; how salts, stereoisomers, conjugates, and in-product conversion are treated; how multi-unit packages are aggregated; what sampling plan applies; the validated analytical method; the limit of quantitation; allowable measurement uncertainty; and the enforcement tolerance near the threshold. Without these details, laboratories may reach inconsistent results and manufacturers may design around the rule.

HHS should also protect genuine botanical material from inadvertent classification. Naturally occurring alkaloid content varies by genetics, harvest, storage, oxidation, extraction, and testing method. A safe harbor should be based on validated distributions from independently sampled botanical products and should not permit products deliberately enriched after extraction to claim botanical status. Conversely, a naturally variable leaf product should not become Schedule I because of ordinary analytical uncertainty at the boundary.

IV. Raw report counts should not be presented as incidence rates

DEA and FDA cite poison-center, FAERS, DEA TOX, NFLIS, case-report, and state-alert data. Together they establish an emerging signal. Each system has a different purpose and ascertainment process. Poison-center coding specific to 7-OH was implemented during 2025. FAERS is voluntary and cannot determine incidence or causation. DEA TOX receives selected submissions and is not a census of overdose deaths. NFLIS reflects evidence submitted to participating laboratories and may be affected by testing practices. [R1,R3,R7-R8]

HHS should require agencies to report, for each series, the case definition, coding start date, testing method, geographic coverage, deduplication method, missing-data rate, suspected product type, co-exposures, and overlap with other systems. Statements about “rapidly increasing abuse” should be limited to what the data establish: rapidly increasing reports or detections under changing surveillance conditions. A rate requires a denominator.

V. Fatal-case detection must be distinguished from causal attribution

DEA’s notice reports 55 fatal DEA TOX cases with 7-OH detection. The later DEA special report on broader kratom-related detections reports 111 fatal cases through April 2026. In that special report, 171 of 182 specimens, 94%, had at least one non-kratom co-detection, with a median of seven; fentanyl was detected in 34% of whole-blood samples. These findings are important, but they do not identify how many deaths were caused solely, primarily, or materially by 7-OH. [R1,R7]

HHS should request and publish a privacy-protected fatality line list containing age, sex, state, year, product evidence, matrix, concentrations, analytical method, mitragynine and pseudoindoxyl results, all co-detections, scene and autopsy findings, official cause and manner of death, and the medical examiner’s assessment of each substance’s contribution. It should also report duplicates and overlap among DEA TOX, FAERS, poison centers, published cases, and state alerts. Until such a review is available, the scientifically accurate phrase is “fatal cases in which 7-OH was detected,” not “deaths caused by 7-OH.”

This distinction does not imply that 7-OH was irrelevant. Polysubstance combinations can be causal, and 7-OH may have contributed in some cases. It simply prevents the administrative record from converting toxicologic presence into an attributable-death count without the necessary adjudication.

VI. National overdose trends neither prove safety nor support a simple causal emergency narrative

National overdose deaths fell from 107,941 in 2022 to 105,007 in 2023 and 79,384 in 2024; provisional 2025 data report 69,973. Opioid-involved deaths also fell. Concentrated 7-OH products became more visible during roughly 2023 and 2024. These ecological data do not establish that 7-OH reduced deaths, because many determinants of overdose changed simultaneously. They also do not support a simple assertion that 7-OH market entry produced an increasing national overdose-death trend. [R9-R12]

The relevant policy question is product-specific and exposure-adjusted: among otherwise comparable people, does use of verified concentrated 7-OH increase or decrease fatal and nonfatal overdose, illicit fentanyl exposure, pain and function, treatment entry, and dependence? The present record does not answer that question.

VII. The substitution hypothesis is plausible but unproven for concentrated 7-OH

Surveys, qualitative studies, ecological-momentary assessment, and case reports indicate that some people use botanical kratom to manage pain, reduce prescription-opioid use, or self-treat opioid withdrawal. These findings make substitution plausible and deserve serious study. They are not proof that concentrated 7-OH is a safe or effective harm-reduction product. The studies generally rely on self-selected respondents and unverified products and lack appropriate comparison groups. [R35-R43]

HHS should not infer a benefit for concentrated 7-OH from botanical-kratom evidence. It should also avoid assuming that removing concentrated 7-OH cannot produce substitution in the opposite direction. A prospective study should compare verified botanical kratom, verified concentrated 7-OH, evidence-based medications for opioid use disorder, and other real-world choices, using serial toxicology and overdose outcomes. Policy should remain revisable as those data emerge.

VIII. HHS should evaluate a rapid, enforceable alternative-control package

The choice is not limited to the current unregulated market or Schedule I. HHS should evaluate whether the following combined controls can address the identified mechanisms of harm:

Minimum age 21, robust online age verification, no vending-machine sales, and meaningful compliance checks.

Federal or interoperable state licensing of manufacturers, distributors, online sellers, and retailers, with recall and audit authority.

Drug-like GMP or strengthened dietary-supplement GMP, batch records, supplier qualification, and stability testing.

Independent ISO/IEC 17025-accredited testing using a validated LC-MS/MS method, with lot-specific public certificates of analysis and measurement uncertainty.

Precautionary limits on 7-OH per unit, serving, and container, plus an anti-circumvention aggregation rule; any limit should be labeled an interim risk-management threshold rather than a proven safe dose.

Front-of-package opioid warnings; exact 7-OH milligrams per unit, serving, and container; warnings against alcohol, benzodiazepines, opioids, gabapentinoids, driving, pregnancy, and use by opioid-naive individuals; and naloxone information.

Child-resistant, tamper-evident, non-candy packaging; no cartoons, candy mimicry, or youth-oriented flavors and imagery.

A prohibition on inhaled, intranasal, or other rapid-delivery forms and on co-formulation with CNS depressants, stimulants, tianeptine, phenibut, yohimbine, mitragynine pseudoindoxyl, or undisclosed psychoactive alkaloids.

Mandatory reporting of serious adverse events and mandatory reporting of units and total milligrams sold by state, so event rates can be calculated.

A time-limited behind-counter or pharmacy-only pilot with counseling, purchase limits, naloxone access, and referral to pain care or medication treatment.

No single measure is sufficient. A weak voluntary code would not answer the concern. The alternative should be compared with temporary Schedule I using predicted effects on initiation, dependence, poisonings, fatalities, treatment demand, illicit substitution, enforcement feasibility, and research access.

IX. If temporary scheduling proceeds, transition and research protections are essential

Abrupt removal could cause withdrawal in physically dependent consumers and may shift some people toward counterfeit products, novel analogs, or illicit opioids. The magnitude is unknown, but the risk is foreseeable. HHS should coordinate clear public communication, low-barrier buprenorphine access, naloxone distribution, poison-center guidance, clinician education, and active surveillance of treatment and overdose outcomes. Historical evidence from opioid reformulation and other drug controls shows that restrictions can reduce one product while encouraging substitution among some users. The analogy is not proof of what will happen here; it is a reason to measure total harm. [R49-R55]

HHS should also recommend streamlined Schedule I research registration, standardized reference materials, grants for human pharmacology and epidemiology, and protection for existing lawful research inventories. A public reassessment should occur within six to twelve months using predefined indicators, not only at the end of the temporary-scheduling period.

X. Specific requests

1. Publish the scientific derivation and analytical validation for the 0.050% and 1.00-milligram thresholds.

2. Adopt definitions and measurement rules that distinguish genuine botanical material from deliberately enriched or semi-synthetic products.

3. Release a deidentified case-level mortality dataset and deduplication analysis.

4. Require manufacturers and sellers to report units and total milligrams sold, enabling exposure-adjusted rates.

5. Commission a formal comparative analysis of Schedule I and the combined alternative-control package described above.

6. Create a transition, treatment, naloxone, and illicit-substitution monitoring plan before any order becomes effective.

7. Facilitate research and commit to a six- to twelve-month public reassessment against predefined epidemiologic criteria.

XI. Conclusion

Concentrated 7-OH should not remain in an opaque, youth-accessible, high-dose retail market. The evidence supports decisive regulation. It does not yet quantify the national burden or demonstrate that Schedule I is the

uniquely necessary and least harmful intervention. HHS can protect public health more effectively by insisting on transparent causal language, validated thresholds, exposure denominators, case-level mortality review, enforceable product and retail controls, research access, and a plan to detect unintended substitution.

Respectfully submitted,

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Public Narrative Summary

By July 2026, a molecule once discussed mostly in kratom chemistry papers had become the center of a federal scheduling fight. 7-hydroxymitragynine, 7-OH, was being sold in tablets, gummies, shots, and dissolvable products at smoke shops and online. Some labels advertised doses that bore little resemblance to the trace amounts naturally present in kratom leaf. Users described fast pain relief, energy, calm, or escape from other opioids. Clinicians described something else: people redosing every few hours, waking in withdrawal, or seeking buprenorphine after their use accelerated. Regulators saw an emerging opioid market growing faster than the evidence needed to govern it.

On July 6, the Drug Enforcement Administration published notice that it intended to place 7-OH above a specified threshold into Schedule I temporarily. The earliest effective date is August 5, 2026. The order, if issued, could last two years and be extended for a third while permanent scheduling proceeds. The proposal is designed to leave qualifying botanical kratom outside the order while capturing material above 0.050% 7-OH and processed products containing more than 1 milligram per article. [R1,R4]

The fight is often framed as a binary: either 7-OH is a lifesaving alternative to fentanyl, or it is the next fentanyl and must be removed immediately. The evidence supports neither slogan. It shows a pharmacologically real opioid with credible risks of addiction and respiratory depression. It also shows a federal record built largely from animal experiments, selected toxicology cases, voluntary reports, poison-center calls, product scans, and a small number of human case reports. Those sources can identify danger. They cannot yet tell the country how common use is, how many doses have been consumed, how often serious harm occurs, or how many cited deaths were actually caused by 7-OH.

The core policy question is not whether concentrated 7-OH is harmless. It is whether Schedule I is the only effective way to reduce its harm, and whether the government has measured what happens next.

The molecule and the market are not the same thing

Kratom is a plant, Mitragyna speciosa, whose leaves contain many alkaloids. Mitragynine is usually the dominant one. 7-OH is naturally present at far lower levels and can also be formed when the body metabolizes mitragynine. Modern concentrated products change that relationship. Manufacturers may enrich, isolate, oxidize, or otherwise produce much larger amounts of 7-OH and deliver them in small, convenient units. Product testing and marketing research has found labels ranging from roughly 1 to 700 milligrams per serving. Some products are sold with candy-like flavors, bright graphics, or claims that blur the line between a botanical supplement and a fast-acting opioid product. [R13-R14,R23-R26]

That distinction matters in both directions. Evidence that traditional kratom leaf may carry a lower acute respiratory risk than conventional full opioid agonists cannot simply be assigned to concentrated 7-OH. Nor can a severe event involving a high-dose 7-OH tablet be treated as evidence about every cup of kratom tea. FDA's own assessment makes the distinction, warning that enriched products are pharmacologically and toxicologically different from ordinary botanical material. [R3]

Known fact: 7-OH activates the mu-opioid receptor, the same receptor system central to morphine, oxycodone, heroin, and fentanyl. In animals, it produces analgesia, reward or reinforcement, morphine-like drug discrimination, tolerance, physical dependence, withdrawal, and respiratory depression. [R15-R22] Reasonable inference: a consumer product that rapidly delivers high doses can create meaningful addiction and overdose risk. Unknown: the human dose-response curve, therapeutic index, chronic toxicity, and comparative fatality risk of the commercial products now on shelves.

What the human evidence actually shows

The most direct human evidence for concentrated 7-OH is not a clinical trial. It is a set of case reports and small treatment series. One report describes inpatient medically managed withdrawal. Another describes a person using about 360 milligrams a day who stopped for roughly two days and was treated with buprenorphine/naloxone. A 2026 report describes 7-OH use disorder treated with buprenorphine after withdrawal appeared within hours. A nine-patient retrospective telehealth series suggests that buprenorphine initiation can work for selected patients. [R28-R31]

These cases are clinically valuable because they answer a threshold question: can concentrated 7-OH produce opioid-like dependence severe enough to require treatment? Yes. They do not answer how often that happens. Patients in case reports are selected precisely because something went wrong, and a nine-person treatment series cannot estimate risk among the much larger unknown universe of consumers. The cases also vary in product verification, dose accuracy, co-use, and follow-up.

A separate case report describes cardiopulmonary arrest after reported 7-OH use and recovery after naloxone. That pattern is consistent with opioid-mediated respiratory toxicity. It is not a population study, and a single case cannot define a general fatal dose or prove that no other factor contributed unless exposure and co-exposures were comprehensively verified. [R32] Another report cited by DEA involved extreme psychosis and self-amputation in the context of cannabis and kratom. Describing it as isolated “7-OH-induced psychosis” strips away the multifactorial facts identified in the published report. [R33]

Known fact: clinically important dependence, withdrawal, and severe toxicity can occur. Reasonable inference: high-frequency dosing and rapid-onset formulations may increase reinforcement and withdrawal cycling. Unknown: the proportion of users who develop a substance use disorder, the rate of nonfatal overdose, and whether risk differs by dose, route, product composition, or prior opioid tolerance.

The surveillance systems are flashing, but they do not measure the same thing

DEA and FDA assembled evidence from multiple systems: poison centers, FDA adverse-event reports, DEA toxicology submissions, forensic laboratory reports, published cases, and state alerts. That convergence should not be dismissed. A signal appearing in different systems is more credible than one isolated anecdote. It is one reason immediate regulation is justified. [R1,R3,R7-R8]

But each system has a different blind spot. Poison centers depend on someone calling and accurately identifying a product. A specific 7-OH code was implemented only during 2025, so later counts benefited from recognition and coding that earlier years lacked. FDA’s Adverse Event Reporting System is voluntary; reports can be incomplete, duplicated, stimulated by publicity, or unable to separate the suspect product from other drugs. DEA TOX receives selected specimens from participating agencies rather than every overdose death. NFLIS records evidence submitted to laboratories, not people using a product. These are signal-detection tools, not incidence surveys.

The missing quantity is the denominator. Regulators have counts of calls, reports, detections, and products. They do not publicly report the number of unique users, units sold, total milligrams sold, doses consumed, or person-years of exposure. If adverse reports double while sales increase tenfold, risk per exposure may be falling. If reports double while sales are stable, risk may be rising. Without the denominator, both stories fit the same numerator.

This does not make the reports meaningless. It changes the language they can support. “Reports increased rapidly” is defensible. “The rate of overdose increased rapidly” is not, unless exposure and ascertainment are measured. “7-OH was detected in fatal cases” is defensible. “7-OH caused every cited death” is not, unless each case is adjudicated.

Fifty-five fatal cases, and a much harder question

DEA's notice says its toxicology program had identified 85 7-OH cases since 2019, including 55 fatal and 30 nonfatal cases. The number is alarming at first glance. Yet the public notice does not provide a deidentified line list showing what happened in each death, what else was present, whether a product was found, what the autopsy showed, or what the medical examiner listed as the cause. [R1]

A newer DEA special report, covering broader kratom-related detections through April 2026, makes the interpretive problem visible. It describes 166 cases and 182 samples, including 111 fatal cases. In 171 of 182 samples, 94%, at least one non-kratom substance was also detected. The median was seven co-detections, with a range up to 22. Fentanyl appeared in 34% of whole-blood samples; naloxone, gabapentin, antidepressants, stimulants, and other drugs also appeared frequently. [R7]

Polysubstance evidence does not absolve 7-OH. Multiple drugs can act together, and an opioid may be a material contributor even when it is not the only substance present. But co-detections make aggregate causal attribution impossible. A proper fatality audit would need the toxicology matrix and concentration, validated assay, timing, scene evidence, product testing, autopsy, medical history, all co-intoxicants, and the official cause and manner of death. It would also need to identify duplicate cases appearing in DEA TOX, FAERS, poison-center data, published reports, and state alerts.

The most detailed published fatality in the cited literature predates the current concentrated-product market. In the 2014 Karinen case, a middle-aged man had mitragynine, 7-OH, and therapeutic-range concentrations of zopiclone, citalopram, and lamotrigine. The authors concluded that kratom alkaloid intoxication was the main cause. That is evidence that kratom alkaloids can contribute to fatal poisoning. It is not a death from isolated modern 7-OH, and it does not establish how often similar events occur. [R34]

Known fact: 7-OH has been detected in fatal investigations, and fatal contribution is biologically plausible. Reasonable inference: some deaths likely involved a material contribution from 7-OH, especially where opioid toxidrome and exposure evidence align. Unknown: how many deaths were caused solely by 7-OH, how many were primarily caused by it, and the fatality rate per exposure. The scientifically responsible answer is "unknown," not "zero" and not "55."

What happened to U.S. overdose deaths while 7-OH expanded?

The national overdose curve creates an uncomfortable fact for simplistic narratives. U.S. overdose deaths climbed from 67,367 in 2018 to 107,941 in 2022. Then they fell: 105,007 in 2023, 79,384 in 2024, and a provisional 69,973 in 2025. Opioid-involved deaths declined as well. The CDC category dominated by illicit fentanyl, "synthetic opioids other than methadone", fell sharply in 2024. [R9-R12]

Concentrated 7-OH products became conspicuous during roughly 2023 and 2024, the same period in which national deaths were beginning to fall. That timing does not prove benefit. Ecological trends are shaped by naloxone distribution, treatment access, changes in illicit supply, prevention programs, patterns of xylazine and stimulant use, demographic change, and countless local interventions. Market entry is also not a clean date, and national totals can conceal local or subgroup harms.

Still, the decline matters because it limits what can honestly be claimed. The available national data do not show a rising overdose-death wave following 7-OH's commercial expansion. A product-specific emergency may exist even during a national decline, but regulators should say so precisely. The emergency case rests on the molecule, product design, and increasing reports, not on evidence that 7-OH caused national overdose mortality to rise.

Could people be substituting 7-OH or kratom for fentanyl?

For years, people who use kratom have reported using it for pain, to reduce prescription opioids, or to manage withdrawal from heroin or other opioids. Large online surveys, qualitative interviews, ecological-momentary assessment, and case reports repeat that theme. Some participants report improved function or reduced use of higher-risk drugs. Others report dependence, escalating frequency, or difficult withdrawal. [R35-R43]

This evidence makes substitution plausible, especially for botanical kratom. It does not establish a net mortality benefit. Online surveys attract people motivated to discuss kratom and usually cannot verify the product, prior opioid exposure, or current fentanyl use. Respondents who benefited may be overrepresented; poison-center and treatment samples overrepresent harm. Neither is a random sample. Most studies do not distinguish leaf, extracts, and newer concentrated 7-OH products.

Concentrated 7-OH may be particularly ambiguous as a harm-reduction product. A predictable oral unit could be less dangerous than an illicit fentanyl bag of unknown potency. But a rapid, high-dose opioid sold without medical supervision can also create new dependence, sustain compulsive use, and be combined with sedatives. Both mechanisms are plausible. The net effect is an empirical question.

Answering it would require more than another survey. Researchers would need a prospective cohort of people using fentanyl, heroin, or prescription opioids who choose verified botanical kratom, verified concentrated 7-OH, medication treatment such as buprenorphine or methadone, or another path. Products would need laboratory confirmation. Serial toxicology would need to measure continued fentanyl exposure. Outcomes would include fatal and nonfatal overdose, emergency care, pain and function, withdrawal, substance-use-disorder symptoms, treatment entry, and quality of life. Without that design, the substitution claim remains a hypothesis.

What “imminent hazard” means in law

Temporary scheduling is not a conventional scientific verdict. Under 21 U.S.C. section 811(h), DEA may temporarily place a substance in Schedule I when doing so is necessary to avoid an imminent hazard to public safety. For this accelerated process, the agency considers the history and current pattern of abuse, the scope, duration and significance of abuse, and risk to public health, along with HHS’s comments. It does not have to complete the full permanent-scheduling analysis first. [R4]

The statute does not define imminent hazard as a minimum number of deaths or require definitive causal epidemiology. In Touby v. United States, the Supreme Court upheld the framework, emphasizing the criteria Congress supplied. The law is deliberately preventive. That means critics overreach when they say incomplete evidence automatically makes temporary scheduling unlawful. [R6]

But law and science ask different questions. The statute may permit action under uncertainty; science can still identify what the record has not established. DEA can reasonably conclude that waiting carries risk. HHS can still demand a reproducible basis for the threshold, accurate causal language, and evidence that Schedule I is preferable to other emergency controls. “The agency may act” is not the same as “the agency has selected the best policy.”

The strongest case for Schedule I

The best argument for DEA’s position begins with prevention, not body counting. A potent opioid has entered ordinary commerce in products with inconsistent labels, unknown manufacturing, no approved indication, no controlled human safety study, no standardized dose, and no mature surveillance. Animal data already establish reward, dependence, and respiratory depression. Human cases show withdrawal and severe toxicity. Reports are rising across several systems. Waiting for a randomized trial or a large death toll could mean waiting until the market is entrenched.

Schedule I can rapidly remove products from lawful retail shelves, create federal enforcement authority, and signal to consumers that "natural" branding does not neutralize opioid pharmacology. The proposed threshold attempts to protect ordinary botanical kratom rather than sweeping in the plant indiscriminately. The temporary period could create time for research and permanent rulemaking.

That argument cannot be dismissed as hysteria. There is no serious evidence-based rebuttal to three propositions: concentrated 7-OH has real opioid hazard; the current market lacks safeguards; and more people could be harmed if nothing changes. The dispute is narrower and harder: whether a ban will reduce total harm more than a strict regulated-access system, and whether the federal government is prepared for dependence, substitution, counterfeit products, and research barriers after removal.

The alternatives are stricter than the status quo

Opponents of Schedule I weaken their case when they defend the current market. Brightly packaged opioid products with vague labels and uncertain composition do not become responsible harm reduction merely because some consumers prefer them to fentanyl. A credible alternative must be enforceable and drug-like, not a voluntary industry pledge.

A rapid control package could set a minimum age of 21; require robust online age verification; prohibit vending machines, candy mimicry, and youth-oriented graphics; license every manufacturer, distributor, online seller, and retailer; require drug-like good manufacturing practices; mandate independent accredited testing and public lot certificates; and give regulators recall and inspection authority. Labels should disclose exact 7-OH milligrams per unit, serving, and container and carry plain warnings about dependence, respiratory depression, pregnancy, driving, and mixing with alcohol, benzodiazepines, fentanyl, gabapentinoids, or other sedatives.

Regulators could set precautionary caps per unit, serving, and package, with an anti-circumvention rule that aggregates multiple small pieces. They could prohibit inhaled, intranasal, and other rapid-delivery forms and bar co-formulation with other psychoactive drugs or undisclosed alkaloids. Behind-counter or pharmacy-only sales could add counseling, purchase limits, naloxone, and referral to pain care or medication treatment. None of these measures makes 7-OH safe. Together, they address the exact features that make the present market dangerous.

Most important, manufacturers and sellers should be required to report units and total milligrams sold by state. Serious adverse events should be mandatory, and laboratory-confirmed emergency cases should be tracked under a stable definition. That would finally allow rates per unit, dose, user, and person-time rather than a debate conducted entirely with numerators.

What history warns about bans

Drug-policy history offers analogies, not predictions. When abuse-deterrent OxyContin was introduced, misuse of that formulation fell, but studies documented substitution toward heroin and other illicit opioids among some users. Restrictions on prescription opioids occurred alongside the rise of illicit fentanyl, although the causal story is complex and cannot be reduced to one policy. Scheduling synthetic cannabinoids was followed by rapid turnover to new analogs with unpredictable potency. Novel synthetic opioids continue to appear despite control of earlier compounds. [R49-R54]

These examples do not prove that 7-OH scheduling will send users to fentanyl. The populations, markets, and drugs differ. They establish a narrower lesson: removing one product can change what people buy rather than eliminate why they use it. A policy that measures only the disappearance of labeled 7-OH could look successful even if withdrawal, counterfeit products, pseudoindoxyl analogs, or fentanyl exposure increase.

The country can prepare for that possibility without accepting the status quo. Before any order takes effect, agencies could publish withdrawal guidance, alert clinicians, expand low-barrier buprenorphine access, distribute

naloxone, and warn consumers against unknown replacement products. Laboratories could intensify surveillance for pseudoindoxyl, MGM compounds, and new analogs. States could report changes in poison calls, emergency visits, treatment demand, seizures, and overdose. The policy should be judged by total health outcomes, not by enforcement counts alone.

The threshold is more than a number

HHS's public request focuses heavily on whether the proposed threshold properly distinguishes botanical material from concentrated products. That technical question could determine who becomes a consumer, a regulated seller, or a federal felon. The record needs to explain whether 0.050% and 1 milligram are toxicological breakpoints, distributions observed in natural leaf, analytical limits, enforcement compromises, or some mixture of those rationales. [R2]

A workable rule must define botanical material, extract, enriched, synthetic, semi-synthetic, article, serving, and package. It must specify dry-weight or as-sold measurement, sampling plans, laboratory validation, limit of quantitation, measurement uncertainty, and treatment of salts, isomers, and in-product conversion. It must prevent a manufacturer from dividing a high-dose package into dozens of nominal "articles," while protecting ordinary leaf from being swept into Schedule I because of natural variability near the cutoff.

Known fact: the threshold is intended to separate ordinary botanical material from enhanced products. Reasonable inference: a dual concentration-and-absolute-dose system is harder to evade than either measure alone. Unknown: whether the chosen numbers map to a demonstrated human risk boundary. The government should call them precautionary control thresholds unless and until human evidence supports a "safe versus dangerous" interpretation.

A more honest regulatory conclusion

The strongest evidence does not support complacency. Concentrated 7-OH is not just "kratom but stronger." It is an opioid product category capable of producing dependence and severe toxicity, sold in a market that lacks the safeguards expected for drugs with comparable pharmacology. Immediate action is warranted.

The economics of acting without a denominator

Public-health decisions are often made before perfect evidence exists, but they still require an explicit model of benefits, costs, and uncertainty. The benefit side of temporary scheduling is straightforward in principle: fewer legal retail purchases, fewer new initiations, less exposure to mislabeled high-dose products, and potentially fewer poisonings. The cost side is less visible because it falls across different systems: enforcement and laboratory capacity, treatment for withdrawal, lost access for people using the product for pain, substitution into illicit markets, and delayed research. A policy can reduce the target product while increasing total social cost if users move to something more lethal.

Without sales and user denominators, even a basic cost-effectiveness analysis is impossible. Agencies cannot calculate serious events per million units, per kilogram of 7-OH sold, or per thousand regular users. They cannot estimate how many poisonings a dose cap might prevent, how many consumers would be affected by behind-counter access, or how much enforcement would be required to suppress an online market. Raw adverse-event counts reveal that harm exists, but they do not tell policymakers which intervention produces the largest health gain per dollar or the lowest unintended harm.

A better economic framework would compare at least three scenarios: continued unregulated sales; strict regulated access; and temporary Schedule I. Each scenario would project initiation, dependence, overdose, treatment entry, illicit substitution, enforcement costs, research delays, and consumer impacts under a range of

assumptions. Because the evidence is uncertain, the analysis should use sensitivity ranges rather than a single point estimate. If Schedule I remains superior even under assumptions favorable to regulated access, the case becomes stronger. If the result flips with modest assumptions about substitution, the government should know that before implementation.

Research access is a public-health variable, not an academic footnote

Schedule I does not make research legally impossible, but it adds registration, security, sourcing, and protocol burdens that can slow studies and discourage investigators. That matters because nearly every unresolved policy question is empirical: human respiratory effects, withdrawal treatment, dose-response, product conversion, comparative risk, and substitution. A temporary order intended to buy time should not consume that time by making the needed research harder to launch. [R4,R63]

DEA and HHS could pair any order with expedited research registration, standardized reference material, clear handling rules for seized or preexisting products, targeted grants, and a public research agenda. They could also require manufacturers or laboratories holding composition data to submit it in a usable form. The goal should be to replace uncertainty quickly, not merely to freeze the market while the same questions remain unanswered two years later.

The same evidence does not support certainty. The country does not know how many people use concentrated 7-OH, how many doses have been consumed, the rate of serious harm, or how many cited deaths were caused by it. It does not know whether some opioid-experienced users substitute it for fentanyl, whether opioid-naive consumers are being newly recruited, or what abrupt removal will do. It has not publicly compared a strict regulated-access model with temporary Schedule I.

The most responsible position is therefore neither “ban nothing” nor “the science is settled.” It is to regulate now, measure what matters, publish the case-level evidence, preserve a genuine botanical distinction, create a transition and treatment plan, and make the policy revisable. If DEA concludes that only Schedule I can contain the immediate risk, it should still build those protections into implementation and define the evidence that would justify continuing, modifying, or ending the order.

The United States has repeatedly learned that drug policy can succeed against a molecule while failing the people who use it. 7-OH offers a chance to do better: acknowledge the opioid hazard without inflating the death count, acknowledge plausible substitution without declaring a miracle, and demand a denominator before turning an alarming signal into a population claim. The science is sufficient to act. It is not sufficient to stop asking what the action will cause.

Appendix: Evidentiary Boundaries and Source List

Unsupported Conclusion	Record-Supported Finding	Reason
7-OH caused the national overdose decline.	National overdose deaths declined during the period commercial 7-OH became more visible, but ecological data cannot establish causation.	Protects credibility.
7-OH caused 55 deaths.	DEA reported fatal toxicology detections; public materials do not adjudicate sole or primary causation.	Detection is not causation.
No one has died from 7-OH.	Fatal contribution is biologically plausible, but the sole-agent count is unknown.	Avoids overcorrection.
The threshold is a proven safety boundary.	The threshold appears to be a proposed control boundary; HHS should publish its derivation.	Matches the record.

Schedule I will inevitably push users to fentanyl.	Illicit substitution is foreseeable and historically informed but not proven for 7-OH.	Keeps inference explicit.

Principal sources include the HHS/OASH Request for Information; DEA's temporary-scheduling notice; HHS/FDA scientific assessment materials; Regulations.gov public comments; CDC/NCHS overdose mortality data; NPDS and MMWR poison-center reporting; FAERS submissions; DEA TOX and related forensic toxicology reporting; peer-reviewed receptor, animal, toxicology, human case, and botanical-kratom survey literature; product-testing and market evidence; and the statutory framework in 21 U.S.C. section 811(h). Current CDC overdose trend data were rechecked during preparation. Regulations.gov returned an API rate-limit response during the latest pass, so this submission retains the last successful API public-comment counts from the immediately prior retrieval and labels them as API-retrieved counts rather than live page counts.