FOR FURTHER INFORMATION CONTACT: Quyen Tran, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Room 5324, Silver Spring, MD 20993–0002, 301–796–2771, *Quyen.Tran1@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION: FDA is announcing the issuance of a priority review voucher to the sponsor of an approved rare pediatric disease product application. Under section 529 of the FD&C Act (21 U.S.C. 360ff), FDA will award priority review vouchers to sponsors of approved rare pediatric disease product applications that meet certain criteria. FDA has determined ZYCUBO (copper histidinate), manufactured by Sentynl Therapeutics Inc., meets the criteria for a priority review voucher. ZYCUBO (copper histidinate) injection is indicated for treatment of Menkes disease in pediatric patients.

For further information about the Rare Pediatric Disease Priority Review Voucher Program and for a link to the full text of section 529 of the FD&C Act, go to *https://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/RarePediatricDiseasePriorityVoucherProgram/default.htm.* For further information about ZYCUBO (copper histidinate), go to the ''*Drugs@FDA*'' website at *https://www.accessdata.fda.gov/scripts/cder/daf.*

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

[FR Doc. 2026–03925 Filed 2–26–26; 8:45 am]

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2026–N–1628]

International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; Scheduling Recommendations; N-Pyrrolidino Isotonitazene; N-Desethyl Etonitazene; Coca Leaf; MDMB-FUBINACA; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice; request for comments.

SUMMARY: The Food and Drug Administration (FDA or Agency) is providing interested persons with the opportunity to submit written comments concerning recommendations to impose international manufacturing and distributing restrictions on certain drug substances, under international drug control treaties. The comments received in response to this notice will be considered in preparing the United States' position on these proposals for a meeting of the United Nations Commission on Narcotic Drugs (CND) in Vienna, Austria, in March 9–13, 2026. This notice is issued under the Controlled Substances Act (CSA).

DATES: Submit either electronic or written comments by March 5, 2026.

ADDRESSES: You may submit comments as follows. Please note that late, untimely filed comments will not be considered. Electronic comments must be submitted on or before March 5, 2026. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of March 5, 2026. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2026–N–1628 for ''International Drug Scheduling; Convention on Psychotropic Substances; Single Convention on Narcotic Drugs; Scheduling Recommendations; *N*-Pyrrolidino isotonitazene; *N*-Desethyl etonitazene; Coca leaf; MDMB-FUBINACA; Request for Comments.'' Received comments, those filed in a timely manner (see), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the

''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.

FOR FURTHER INFORMATION CONTACT: Edward (Greg) Hawkins, Center for Drug Evaluation and Research, Controlled Substance Staff, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 5110, Silver Spring, MD 20993–0002, 301–796–0727, *Edward.hawkins@fda.hhs.gov.*

SUPPLEMENTARY INFORMATION:

I. Background

The United States is a party to the 1971 Convention on Psychotropic Substances (1971 Convention). Section 201(d)(2)(B) of the CSA (21 U.S.C. 811(d)(2)(B)) provides that when the United States is notified under Article 2 of the 1971 Convention that the CND proposes to decide whether to add a drug or other substance to one of the schedules of the 1971 Convention, transfer a drug or substance from one schedule to another, or delete it from the schedules, the Secretary of State must transmit notice of such information to the Secretary of Health and Human Services (Secretary of HHS). The Secretary of HHS must then publish a summary of such information in the **Federal Register** and provide opportunity for interested persons to submit comments. The Secretary of HHS must then evaluate the proposal and the comments received from interested persons, and furnish a recommendation to the Secretary of State that shall be binding on the representative of the United States in discussions and negotiations relating to the proposal.

As detailed in the following paragraphs, the Secretary of State has received notification from the Secretary-General of the United Nations (the Secretary-General) regarding one substance to be considered for control under the 1971 Convention. Section 201(d)(2)(B) of the CSA requires the Secretary of HHS, after receiving a notification proposing scheduling, to publish a notice in the **Federal Register** to provide the opportunity for interested persons to submit information and comments on the proposed scheduling action.

The United States is also a party to the 1961 Single Convention on Narcotic Drugs (1961 Convention). The Secretary of State has received a notification from the Secretary-General regarding three substances to be considered for control under this convention. The CSA does not require HHS to publish a summary of such information in the **Federal Register**. Nevertheless, to provide interested and affected persons an opportunity to submit comments regarding the recommendations for drugs under the 1961 Convention, the notification regarding these substances is also included in this **Federal Register** notice. The comments will be shared with other relevant Agencies to assist the Secretary of State in formulating the position of the United States on the control of these substances. The HHS recommendations are not binding on the representative of the United States in discussions and negotiations relating to the proposal regarding control of substances under the 1961 Convention.

II. United Nations Notification

The United Nations identified the drug substances and explains the basis for the scheduling recommendations as follows:

Substances Recommended To Be Added to Schedule I of the Single Convention (1961)

—*N*-Pyrrolidino isotonitazene
IUPAC name: 5-Nitro-2-[4-(2-propoxy)benzyl]-1-[2-pyrrolidin-1-yl]-1*H*-benzo[d]imidazole
Alternate names: Isotonitazepyne
—*N*-Desethyl etonitazene
IUPAC name: 2-[(4-Ethoxyphenyl)methyl]-*N*-ethyl-5-nitro-1*H*-benzimidazole-1-ethanamine

Substance Recommended To Be Retained in Schedule I of the Single Convention (1961)

—Coca leaf
IUPAC name: n/a

Substance Recommended To Be Added to Schedule II of the Psychotropic Convention (1971)

—MDMB-FUBINACA
UPAC name: Methyl 2-(1-(4-fluorobenzyl)-1*H*-indazole-3-carboxamido)-3,3-dimethylbutanoate

Additional Information Regarding Substances To Be Added to Schedule I of the Single Convention on Narcotic Drugs (1961)

N-Pyrrolidino Isotonitazene

Substance Identification

N-Pyrrolidino isotonitazene (IUPAC name: 5-nitro-2-(4-(2-propoxy)benzyl]-1-[2-(pyrrolidin-1-yl)ethyl]lH-benzo[d] imidazole, also known as isotonitazepyne) is a 5-nitro-2-benzylbenzimidazole synthetic opioid.

N-Pyrrolidino isotonitazene has been described as a crystalline solid and has also been detected in falsified pharmaceuticals, appearing as coloured tablets.

Review History

N-Pyrrolidino isotonitazene has not previously been reviewed and is not currently under international control. Information was brought to the review committees' the attention that the substance is manufactured clandestinely, poses a risk to public health and has no recognized therapeutic use.

Similarity to Known Substances and Effects on the Central Nervous System

The chemical structure and pharmacological effects of *N*-pyrrolidino isotonitazene closely resemble those of *N*-pyrrolidino protonitazene, which is controlled under Schedule I of the Single Convention on Narcotic Drugs of 1961.

Studies in animals have demonstrated that *N*-pyrrolidino isotonitazene is a full agonist at μ-opioid receptors, with greater potency than morphine and fentanyl. Its effects are blocked by the opioid antagonist, naltrexone.

Convertibility Into Controlled Substances

It is not known whether *N*-pyrrolidino isotonitazene can be converted into a controlled substance.

Dependence Potential

No controlled studies of the dependence potential *N*-pyrrolidino isotonitazene in animals or humans have been reported. As it is a potent μ-opioid receptor agonist, it would be expected to produce dependence similar to that of other opioids, such as morphine and fentanyl.

Actual Abuse and/or Evidence of Likelihood of Abuse

In animals, *N*-pyrrolidino isotonitazene had effects suggestive of an abuse potential similar to that of morphine and fentanyl. Its potency was greater than that of morphine and fentanyl. These effects were blocked by the opioid antagonist naltrexone. Euphoria and self-management of opioid withdrawal have been described by people who report its use.

Other Health Harms

The presence of *N*-pyrrolidino isotonitazene has been reported in many countries in many regions, although the extent of use is unknown. *N*-Pyrrolidino isotonitazene has been analytically confirmed in fatal and non-fatal cases of overdose, including in cases in which it was the only substance detected.

Detection of *N*-pyrrolidino isotonitazene in falsified pharmaceutical drugs in many countries and regions indicates a risk of unintentional use and harm.

Therapeutic Usefulness

N-Pyrrolidino isotonitazene is not known to have any therapeutic use.

Recommendation

N-Pyrrolidino isotonitazene, also referred to as isotonitazepyne, is a synthetic opioid that is liable to abuse and produces effects similar to those of other opioids that are controlled under Schedule I of the 1961 Single Convention on Narcotic Drugs. Its use causes substantial harm, including death. It has no known therapeutic use.

Recommendation: The Committee recommended that *N*-pyrrolidino isotonitazene, also referred to as isotonitazepyne, be added to Schedule I of the 1961 Single Convention on Narcotic Drugs.

N-Desethyl Etonitazene

Substance Identification

N-Desethyl etonitazene (IUPAC name: 2-[(4-ethoxyphenyl)methyl]-N-ethyl-5-nitro-lH-

benzimidazole-1-ethana mine) is a 5-nitro-2-benzylbenzimidazole synthetic opioid. *N*-Desethyl etonitazene has been described as a crystalline solid and as a yellow or beige powder. It has been found in falsified pharmaceutical opioid tablets.

Review History

N-Desethyl etonitazene has not previously been reviewed and is not currently under international control. Information was brought to the attention of the reviewers that the substance is manufactured clandestinely, poses a risk to public health and has no recognized therapeutic use.

Similarity to Known Substances and Effects on the Central Nervous System

N-Desethyl etonitazene is a metabolite of etonitazene, which is controlled under Schedule I of the 1961 Convention on Narcotic Drugs.

Studies of receptor binding indicate that *N*-desethyl etonitazene is a full agonist at μ-opioid receptors, with greater potency than morphine and fentanyl.

Convertibility Into Controlled Substances

It is not known whether *N*-desethyl etonitazene can be converted into a controlled substance, although this is theoretically possible.

Dependence Potential

No controlled studies of the dependence potential of *N*-desethyl etonitazene in animals or humans have been reported. As it is a potent μ-opioid receptor agonist, it would be expected to produce dependence similar to that produced by other opioids, such as morphine and fentanyl.

Actual Abuse and/or Evidence of Likelihood of Abuse

The presence of *N*-desethyl etonitazene has been reported in at least 10 countries, although the extent of use is unknown.

Other Health Harms

At least three deaths have been reported in which *N*-desethyl etonitazene was analytically confirmed, including when no other opioids were involved. *N*-Pyrrolidino etonitazene has also been analytically confirmed in non-fatal overdoses. The detection of *N*-pyrrolidino etonitazene in falsified pharmaceutical drugs indicates a risk of unintentional use and harm.

Therapeutic Usefulness

N-Desethyl etonitazene is not known to have any therapeutic use.

Recommendation

N-Desethyl etonitazene is a synthetic opioid that is liable to abuse and produces ill effects similar to those produced by other opioids that are controlled under Schedule I of the 1961 Single Convention on Narcotic Drugs. It could theoretically be converted into a controlled substance, although this has not been demonstrated. Its use causes substantial harm, including death. It has no known therapeutic use.

Recommendation: The Committee recommended that *N*-desethyl etonitazene be added to Schedule I of the 1961Single Convention on Narcotic Drugs.

Substances To Remain in Schedule I of the Single Convention on Narcotic Drugs (1961)

Coca Leaf

Substance Identification

Coca leaf is defined in the 1961 United Nations Single Convention on Narcotic Drugs as the leaf of the coca bush, except when all ecgonine, cocaine and any other ecgonine alkaloid have been removed. ''Coca bush'' refers to the plant of any species of the genus Erythroxylon. ''Coca leaf preparations'' refer to mixtures or products containing the coca leaf (in whole or in part). This excludes isolated alkaloids such as cocaine and ecgonine, which are controlled separately under the Convention.

More than 250 Erythroxylum species exist, including four primary cultivated varieties. Coca leaf cultivation is most prevalent at high altitudes in the Andean region and in the Amazon basin but is increasingly being reported in other parts of the Region of the Americas. Coca leaf is cultivated from plants grown from seeds or cuttings. Plants can produce leaves for 20–30 years.

Coca leaves are similar in appearance to those of *Laurus nobilis,* the most common characteristic trait in all species being a darker color on the upper than on the underside of the leaf and two lines parallel to the midrib of the leaf.

Coca leaf preparations are marketed as branded products. They include teas, nutritional supplements, and essential oil. Coca leaves can be pulverized finely into a greenish powder.

Coca leaf products are traditionally administered by two primary routes: chewing and infusion. Chewing of coca leaves is widespread and culturally accepted in the Andean highlands. The process involves placing a wad of dried leaves in the buccal cavity, either alone or with an alkaline substance such as lime or sodium bicarbonate to enhance extraction of alkaloids into the oral mucosa. Coca leaves are also infused in water and consumed as tea. Coca leaf flour (finely ground coca leaves) can be used to make a strong tea and is sold as a nutritional supplement.

Review History

Coca-leaf chewing was discussed at the 3rd (1952) and 4th (1954) meetings of the Expert Committee on Drugs Liable to Produce Addiction, which concluded that it was a form of addiction. Coca leaf was subsequently placed under Schedule I of the 1961 Single Convention on Narcotic Drugs.

In 1992, a pre-review of coca leaf was conducted and the reviewers considered that coca leaf was appropriately scheduled under the 1961 Convention, as cocaine is readily extractable from the leaf.

In 2023, an official request from a Member State for a critical review of coca leaf. A critical review was initiated, for conclusion in 2025.

Similarity to Known Substances and Effects on the Central Nervous System

Coca leaf contains a mix of alkaloids, flavonoids, terpenes, tannins, and phenols. Cocaine and ecgonine are naturally occurring alkaloids of note in the coca leaf. The total alkaloid content is 0.5–2.4%, depending on the species, growth environment, and stage of leaf development. Cocaine, one alkaloid in the leaf, is produced in significant amounts in cultivated varieties of the Erythroxylum species, whereas wild species contain either none or only small quantities of this alkaloid. When present, the cocaine content of cultivated species varies among regions from 0.11% to 1.02% of the weight of dried coca leaf. Absorption of alkaloids from coca leaf depends on the route of administration, the quantity of leaves used, the type of alkali added, and if masticated, the duration of mastication. The plasma concentrations of cocaine resulting from coca leaf chewing or ingestion may overlap with plasma concentrations of cocaine resulting from cocaine use by inhalation or injection.

It has been demonstrated in animal models that coca leaf alkaloids affect the central nervous system, including decreasing food intake. Some coca leaf extracts increase locomotor activity, while others do not. The stimulant effects of coca leaf in animal models may be due to inhibition of monoamine re-uptake. Local anesthetic effects have also been observed in animal models.

People who chew coca leaf report mild psychostimulant effects, including euphoria, and have described it as an ''energizer''. Increased heart rate and blood pressure and vasoconstriction have also been reported. Analgesic effects of high-dose coca leaf preparations have been attributed to a local anesthetic effect.

Convertibility Into Controlled Substances

Coca leaf contains cocaine, a naturally occurring alkaloid that can be processed to obtain coca paste. Coca paste is filtered and dried to obtain cocaine base, which is further processed to obtain cocaine hydrochloride. By chemical definition, the manufacture of cocaine from coca leaf is an extraction; however, the reference in the Guidance document for the understanding of this term reads as follows:

A substance is convertible if it is of such a kind as to make it, by the ease of the process and by the yield, practicable and profitable for a clandestine manufacturer to transform the substance in question into controlled drugs.

Obtaining coca paste from coca leaf and purification of different forms of cocaine from coca paste are straightforward and do not require special expertise or equipment. Except for kerosene, the chemicals and reagents used in these processes are listed in the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988.

Most coca leaf is used for clandestine manufacture of cocaine in at least some countries. It is estimated that 1 ha of coca bush cultivation produces approximately 4.2 tons of fresh coca leaves per year; 1 ton of fresh leaves produces approximately 1.5 kg of coca paste or 1.4 kg of cocaine base; 1 kg of cocaine base results in roughly 0.9 kg of cocaine hydrochloride, which typically contains about 85% pure cocaine. Cocaine production has increased significantly in several countries, in parallel with increased coca bush cultivation. Some countries have reported historically high levels in recent

years. Globally, a 34% increase in cocaine production was reported in 2023 over the previous year.

The 1961 Convention lists both coca leaf and cocaine as controlled substances under Schedule 1. Accordingly, as coca leaf is used to manufacture cocaine, one controlled substance (cocaine) is made from another (coca leaf), thereby meeting the Convention's criterion for convertibility.

Dependence Potential

No controlled studies in animal models of the dependence potential of coca leaf were identified.

A few studies in humans assessed development of a dependence syndrome with coca leaf. Older ethnographic studies did not describe tolerance, withdrawal symptoms, or compulsive patterns of use; however, a recent epidemiological study of more than 1300 people who chewed coca leaf found that 2.3% of those who reported ever chewing coca leaf met the ICD–10 criterion for dependence.

People who met the criterion had a lower quality of life than people who did not. Two countries in different geographical regions reported presentations for drug dependence treatment related to coca leaf use. No studies were available that provided robust evidence to determine the prevalence of coca leaf dependence.

Actual Abuse and/or Evidence of Likelihood of Abuse

In a model of drug discrimination in animals, high-dose preparations of coca leaf produced effects that closely resembled those of cocaine.

Many countries in various regions have reported nonmedical use of coca leaf and increasing numbers of seizures of coca leaf.

Other Health Harms

Few high-quality data are available on the acute toxicity associated with coca leaf. No fatal overdoses have been documented after traditional use of coca leaf, although coca leaf may not readily be differentiated from cocaine in biological samples from such cases.

Reported adverse effects of chewing coca leaf appear to be limited. They include oral problems (including risk of oral carcinoma) and cardiovascular, intestinal, hormonal, and neurological issues.

Therapeutic Usefulness

The potential therapeutic effects of various Erythroxylum species have been investigated in vitro and in animal models. Recent investigations have been conducted of its antioxidant, antibiotic, anticancer, antihypertensive, antidiabetic, and neuroprotective effects. For example, some Erythroxylum species may have anticancer effects, comparable to those of standard chemotherapy agents in some cases; however, the activity varies with different extracts and cell lines. Similarly, studies in vitro and in vivo show variable but sometimes strong antioxidant and anti-inflammatory effects. In humans, use of E. coca by chewing and drinking tea reduced post-meal glucose in people with no underlying metabolic disorder. Overall, studies in animals and humans suggest that coca leaf may have some therapeutic applications, although the evidence is limited.

Traditional use of coca leaf in Andean regions includes chewing and infusion to increase energy and prevent altitude sickness, although evidence of its usefulness for treating altitude sickness is mixed. Its use as a nutritional supplement is limited by its cocaine content. Use of coca leaf for the manufacture of pharmaceutical and industrial products has decreased with time. In a few countries, preparations of coca leaf are used as traditional herbal medicines. Use of coca leaf is permitted under national legislation in some countries when practiced within traditional or cultural contexts.

Recommendation

The Expert Committee, when deciding whether to recommend international control, decides whether a substance: ''{l) is liable to similar abuse and productive of similar ill-effects as the substances in Schedule I or Schedule II; or (2) is convertible into a substance already in Schedule I or Schedule II.'' The reference in the Guidance document for the understanding of this term reads as follows:

A substance is convertible if it is of such a kind as to make it, by the ease of the process and by the yield, practicable and profitable for a clandestine manufacturer to transform the substance in question into controlled drugs.

In the 1961 Single Convention on Narcotic Drugs, coca leaf is defined as the leaf of the coca bush, except when all ecgonine, cocaine, and any other ecgonine alkaloids have been removed. Coca leaf and cocaine are classified as distinct substances under Schedule I of the 1961 Single Convention. The simplicity of extracting cocaine from coca leaf and its high yield and profitability are well known.

Accordingly, conversion of coca leaf into cocaine constitutes production of one substance (cocaine) in Schedule I from another substance in Schedule I (coca leaf), thereby meeting the Convention's criterion for convertibility. The Committee also reviewed evidence of a marked increase in coca leaf cultivation and in the production of cocaine-related substances, in the context of significant, increasing public health concern about cocaine use. In that context, the Committee considered that reducing or removing existing international controls on coca leaf could pose an especially serious risk to public health.

The evidence presented in the critical review and other information considered by the Committee indicate that traditional coca leaf use by chewing or in tea does not appear to pose a particularly serious public health risk, although the safety of long-term use is not well documented. In addition, it was recognized that coca leaf has an important cultural and therapeutic significance for Indigenous peoples and other communities and that there are exemptions for traditional use of coca leaf in certain national frameworks. Emerging research may support the therapeutic applications of coca leaf; however, the current body of evidence does not provide a robust basis for such use.

Recommendation: The Committee recommended that coca leaf be retained in Schedule I of the 1961 Single Convention on Narcotic Drugs.

Substances To Be Added to Schedule IV of the Psychotropic Convention (1971)

MDMB-FUBINACA

Substance Identification

MDMB-FUBINACA {IUPAC name: Methyl 2-{[1-{4-fluorobenzyl)indazole-3-carbonyl]amino}-3,3-dimethylbutanoate) is a synthetic cannabinoid with a stereogenic centre (C2), which can exist as two stereoisomers (enantiomers): methyl (25)-2-{[1-(4-fluorobenzyl)indazole-3-carbonyl]amino}-3,3-dimethylbutanoate and methyl (2R)-2-{[1-{ 4-fluorobenzyl)i ndazole-3-carbonyl]amino}-3,3-dimethylbutanoate.

MDMB-FUBINACA has been described as a powder (usually white) and has been found sprayed onto herbal products. It is often marketed as dried leaves or powder and sold in e-liquids for vaping.

Review History

MDMB-FUBINACA has not previously been reviewed and is not currently under international control. Information was brought to the reviewers attention that this substance is manufactured clandestinely, poses a risk to public health and has no recognized therapeutic use.

Similarity to Known Substances and Effects on the Central Nervous System

MDMB-FUBINACA is a synthetic cannabinoid that binds to CBl and CB2 receptors with high affinity and is a potent full agonist at both receptors. Its effects are similar to those of other potent CBl agonists that are currently controlled under Schedule II of the Convention on Psychotropic Substances of 1971. No controlled studies of the effects of MDMB-FUBINACA have been reported. In animals, it has been shown to produce behavioral effects consistent with delta-9-THC, with the effects lasting many hours. In humans, it produces symptoms typical of high doses of cannabinoids, including agitation or sedation, vomiting, short-term memory loss, salivation, rhinorrhoea, mydriasis, tachycardia and anxiety.

Convertibility Into Controlled Substances

MDMB-FUBINACA can be chemically modified to produce structurally related synthetic cannabinoids such as ADB-FUBINACA. The yields and prevalence of such conversions are, however, uncertain.

Dependence Potential

No studies of the dependence potential of MDMB-FUBINACA in animals or humans have been reported. Its effects at CB1 receptors suggest that it would produce dependence similar to that produced by delta-9-THC and other synthetic cannabinoid receptor agonists. Countries in two regions reported presentations for treatment of drug dependence due to the use of MDMB-FUBINACA.

Actual abuse and/or evidence of likelihood of abuse:

In an animal model predictive of abuse potential, MDMB-FUBINACA had effects

similar to delta-9-THC. No studies have been conducted to determine the likelihood of abuse of MDMB-FUBINACA in humans.

Other Health Harms

MDMB-FUBINACA use has been associated with mortality and morbidity in several countries, including a large number of non-fatal poisonings. Documented adverse effects include agitation or sedation, vomiting, short-term memory loss, salivation, rhinorrhoea, mydriasis, tachycardia and anxiety, similar to those seen with delta-9-THC and other synthetic cannabinoid receptor agonists. The increased detection of MDMB-FUBINACA has been linked to emergence of a simplified one-step synthesis method, which requires readily available precursor chemicals.

Therapeutic Usefulness

MDMB-FUBINACA is not known to have any therapeutic use.

Recommendation

MDMB-FUBINACA is a synthetic cannabinoid receptor agonist administered by smoking plant material sprayed with the substance or inhaling vapor after heating. Its mode of action suggests the potential for dependence and the likelihood of abuse. Its use has been associated with a range of severe adverse effects, including death. These effects are similar to those produced by other synthetic cannabinoids that are placed in Schedule II of the Convention on Psychotropic Substances of 1971.

MDMB-FUBINACA has no therapeutic use.

Recommendation: The Committee recommended that MDMB-FUBINACA be added to Schedule II of the Convention on Psychotropic Substances of 1971.

III. Discussion

Although specific scheduling recommendations for each of the drug substances have been made, the CND is not obliged to follow those recommendations. Options available to the CND for substances considered for control under the 1971 Convention include the following: (1) accept the recommendations; (2) accept the recommendations to control but control the drug substance in a schedule other than that recommended; or (3) reject the recommendations entirely.

N-Pyrrolidino isotonitazene (isotonitazepyne) is a synthetic opioid of the benzimidazole class that is similar in structure to isotonitazene. In vitro binding and activity data indicate that isotonitazepyne is approximately 10-fold more potent at the mu opioid receptor than fentanyl. Isotonitazepyne has been detected in several toxicology cases in the United States, Europe, and Australia. Common adverse events of opioid agonists include nausea, vomiting, constipation, pruritus, dizziness, sedation, and respiratory depression, where significant respiratory depression can lead to death. Based on in vitro pharmacology and case reports, substances in the nitazepyne class are expected to produce euphoria and have a high potential for abuse and physical dependence. Repeated non-medical use would likely result in tolerance, physical dependence, and withdrawal effects consistent with other potent opioids. There are no commercial uses or approved medical uses for isotonitazepyne in the United States. Isotonitazepyne is controlled in Schedule I under the CSA and will not require additional permanent controls domestically if it is placed in Schedule I of the 1961 Single Convention.

N-Desethyl etonitazene is a synthetic opioid of the nitazene class that is similar in structure to etonitazene. In vitro binding and activity data indicate that *N*-desethyl etonitazene is approximately 10-fold more potent at the mu opioid receptor than fentanyl. In animal behavior studies it produced subjective effects that were indistinguishable from morphine. As a result, it is assumed that metonitazepyne will have an abuse potential similar to that of other opioid agonists and produce adverse events that include nausea, vomiting, constipation, pruritus, dizziness, sedation, and respiratory depression, where significant respiratory depression can lead to death. In the United States, *N*-Desethyl etonitazene was detected in 2 toxicology cases; however, other NPS or other drugs of abuse were detected in these individuals and could have been a contributing factor to the fatality. According to the NFLIS database, *N*-Desethyl etonitazene was first detected in 2023, and there have been seven confirmed law enforcement seizures to date. There are no commercial uses or approved medical uses for *N*-Desethyl etonitazene in the United States. *N*-Desethyl etonitazene is controlled in Schedule I under the CSA and will not require additional permanent controls domestically if it is placed in Schedule I of the 1961 Single Convention.

Coca leaf is defined by the 1961 United Nations Single Convention on Narcotic Drugs as the leaf of the coca bush, except when all ecgonine, cocaine, and any other ecgonine alkaloids have been removed. Coca leaf is consumed through two primary mechanisms (1) direct chewing of the leaves, which also involves placing the leaves in the buccal cavity, and (2) extraction of the alkaloids for oral consumption as through a tea. The coca leaf contains several substances; alkaloids, flavonoids, terpenes, and phenols, several of which either are, or can be easily converted, into substances with known abuse potential and physical dependence. People who chew coca leaves have reported psychostimulant effects such as euphoria and increased energy. The coca leaf contains cocaine, a known stimulant with a high potential for abuse. The coca leaf is used to clandestinely manufacture cocaine which is illicitly distributed throughout the world. In the U.S., federal law enforcement reported seizing more than 91,600 kg of cocaine in the first half of 2025 alone. According to the National Survey on Drug Use and Health, approximately 470,000 U.S. residents age 12 or older reported past-year use of cocaine in 2023, with the National Center for Health Statistics reporting 29,918 overdose deaths involving cocaine in the same year. Cocaine is approved as a nasal and topical analgesic in the U.S., and is controlled in schedule II under the CSA. Coca leaf (leaves), which contains cocaine, is also controlled in Schedule II under the CSA. Domestic scheduling actions on the coca leaf will not be necessary regardless of the outcome of the vote for coca leaf to remain in Schedule I of the 1961 Convention.

MDMB-FUBINACA is a semi-synthetic cannabinoid which functions as an agonist of the cannabinoid 1 (CB1) receptor. MDMB-FUBINACA is reported to produce similar effects as tetrahydrocannabinol (THC) after smoking or oral administration. In animals, MDMB-FUBINACA produced suppression of locomotor activity, analgesia, hypothermia, and ring mobility similar to delta-9-THC. MDMB-FUBINACA also fully substituted for the effects of THC in a drug discrimination study. It was first identified in law enforcement seizures in the U.S. in 2017 and has since been identified in 824 drug seizures. There are no commercial or approved medical uses for MDMB-FUBINACA. MDMB-FUBINACA is controlled in Schedule I under the CSA and will not require additional permanent controls domestically if it is placed in Schedule II of the 1971 Psychotropic Convention.

FDA, on behalf of the Secretary of HHS, invites interested persons to submit comments on the recommendations from the United Nations concerning these drug substances. FDA, in cooperation with the National Institute on Drug Abuse, will consider the comments on behalf of HHS in evaluating the scheduling recommendations. Then, under section 201(d)(2)(B) of the CSA, HHS will recommend to the Secretary of State what position the United States should take when voting on the recommendations for control of

substances under the 1971 Convention at the CND meeting in March 2025.

Comments regarding the recommendations for control of *N*-pyrrolidino isotonitazene, *N*-desethyl etonitazene, and coca leaf under the 1961 Single Convention will also be forwarded to the relevant Agencies for consideration in developing the U.S. position regarding narcotic substances at the CND meeting.

Grace R. Graham,

Deputy Commissioner for Policy, Legislation, and International Affairs.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2023–N–0119]

Fiscal Year 2026 Generic Drug Science and Research Initiatives Workshop; Public Workshop; Request for Comments

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of public workshop; request for comments.

SUMMARY: The Food and Drug Administration (FDA or the Agency) is announcing the following public workshop entitled ''Fiscal Year 2026 Generic Drug Science and Research Initiatives Workshop.'' The purpose of the public workshop is to provide an overview of the status of science and research initiatives for generic drugs and an opportunity for public input on these initiatives. FDA is seeking this input from a variety of interested parties—industry, academia, patient advocates, professional societies, and other interested parties—as it fulfills its commitment under the Generic Drug User Fee Amendments of 2022 (GDUFA III) to develop an annual list of science and research initiatives specific to generic drugs. FDA will take the information it obtains from the public workshop into account in developing its fiscal year (FY) 2027 Generic Drug User Fee Amendments (GDUFA) science and research initiatives.

DATES: The public workshop will be held on June 8 and 9, 2026. Either electronic or written comments on this public workshop must be submitted by July 10, 2026. See the **SUPPLEMENTARY INFORMATION** section for additional information.

ADDRESSES: The public workshop will be held in person and will be accessible virtually (See *Streaming Webcast of the Public Workshop* below). The public workshop will be held at the FDA White Oak Campus, 10903 New Hampshire Avenue, Building 31 Conference Center, the Great Room (Room 1503), Silver Spring, MD 20993. Entrance for the public workshop participants (non-FDA employees) is through Building 1 where routine security check procedures will be performed. For parking and security information, please refer to *https://www.fda.gov/about-fda/visitor-information.*

The procedures to submit comments are outlined below. Please note that late, untimely filed comments will not be considered. The *https://www.regulations.gov* electronic filing system will accept comments until 11:59 p.m. Eastern Time at the end of July 10, 2026. Comments received by mail/hand delivery/courier (for written/paper submissions) will be considered timely if they are received on or before that date.

Electronic Submissions

Submit electronic comments in the following way:

- *Federal eRulemaking Portal: https://www.regulations.gov.* Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to *https://www.regulations.gov* will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on *https://www.regulations.gov.*
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see ''Written/Paper Submissions'' and ''Instructions'').

Written/Paper Submissions

Submit written/paper submissions as follows:

- *Mail/Hand Delivery/Courier (for written/paper submissions):* Dockets Management Staff (HFA–305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in ''Instructions.''

Instructions: All submissions received must include the Docket No. FDA–2023–N–0119 for ''Fiscal Year 2026 Generic Drug Science and Research Initiatives Workshop; Public Workshop; Request for Comments.'' Received comments, those filed in a timely manner (see **ADDRESSES**), will be placed in the docket and, except for those submitted as ''Confidential Submissions,'' publicly viewable at *https://www.regulations.gov* or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240–402–7500.

- Confidential Submissions—To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states ''THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION.'' The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on *https://www.regulations.gov.* Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as ''confidential.'' Any information marked as ''confidential'' will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: *https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.*

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to *https://www.regulations.gov* and insert the docket number, found in brackets in the heading of this document, into the ''Search'' box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240–402–7500.