



## DEPARTMENT OF JUSTICE

### Drug Enforcement Administration

#### 21 CFR Part 1308

[Docket No. DEA1604]

#### Schedules of Controlled Substances: Placement of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA in Schedule I

**AGENCY:** Drug Enforcement Administration, Department of Justice.

**ACTION:** Notice of proposed rulemaking.

**SUMMARY:** The Drug Enforcement Administration proposes placing methyl 2-[[1-(4-fluorobutyl)indole-3-carbonyl]amino]-3,3-dimethylbutanoate (other names: 4F-MDMB-BUTICA; 4F-MDMB-BICA), *N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(pent-4-en-1-yl)-1*H*-indazole-3-carboxamide (other name: ADB-4en-PINACA), ethyl 2-[[1-(5-fluoropentyl)indole-3-carbonyl]amino]-3,3-dimethyl-butanoate (other names: 5F-EDMB-PICA; 5F-EDMB-2201), and methyl 2-(1-(4-fluorobenzyl)-1*H*-indole-3-carboxamido)-3-methyl butanoate (other name: MMB-FUBICA), including their salts, isomers (including optical, positional, and geometric isomers), and salts of isomers, in schedule I of the Controlled Substances Act. 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA were temporarily scheduled in an order dated December 12, 2023. If finalized, this action would make permanent the existing regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis with, or possess) or propose to handle 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA.

**DATES:** Comments must be submitted electronically or postmarked on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER]. The

electronic Federal Docket Management System will not accept comments after 11:59 p.m.

Eastern Time on the last day of the comment period.

Interested persons may file a request for a hearing or waiver of hearing pursuant to 21 CFR 1308.44 and in accordance with 21 CFR 1316.47 and/or 1316.49, as applicable. Requests for a hearing and waivers of an opportunity for a hearing or to participate in a hearing, together with a written statement of position on the matters of fact and law asserted in the hearing, must be received or postmarked on or before [INSERT DATE 30 DAYS AFTER DATE OF PUBLICATION IN THE FEDERAL REGISTER].

**ADDRESSES:** Interested persons may file written comments on this proposal in accordance with 21 CFR 1308.43(g). To ensure proper handling of comments, please reference “Docket No. DEA1064” on all electronic and written correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration (DEA) encourages commenters to submit comments electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the webpage or attach a file for lengthier comments. Please go to <http://www.regulations.gov> and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

- *Paper comments:* Paper comments that duplicate the electronic submissions are not necessary and are discouraged. Should you wish to mail a paper comment in lieu of an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrissette Drive, Springfield, Virginia 22152.

- *Hearing requests:* All requests for a hearing and waivers of participation, together with a written statement of position on the matters of fact and law asserted in the hearing, must be filed with the DEA Administrator, who will make the determination of whether a hearing will be needed to address such matters of fact and law in the rulemaking. Such requests must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrisette Drive, Springfield, Virginia 22152. For informational purposes, a courtesy copy of requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/OALJ, 8701 Morrisette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.

**FOR FURTHER INFORMATION CONTACT:** Dr. Terrence L. Boos, Drug and Chemical Evaluation Section, Diversion Control Division, Drug Enforcement Administration; Telephone: (571) 362-3249.

As required by 5 U.S.C. 553(b)(4), a summary of this proposed rule may be found in the docket for this rulemaking at [www.regulations.gov](http://www.regulations.gov).

**SUPPLEMENTARY INFORMATION:**

The Drug Enforcement Administration (DEA) proposes to permanently schedule the following four controlled substances in schedule I of the Controlled Substances Act (CSA), including their salts, isomers (including optical, positional, and geometric isomers), and salts of isomers whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation:

- methyl 2-[[1-(4-fluorobutyl)indole-3-carbonyl]amino]-3,3-dimethylbutanoate (other names: 4F-MDMB-BUTICA; 4F-MDMB-BICA),
- *N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(pent-4-en-1-yl)-1*H*-indazole-3-carboxamide (other name: ADB-4en-PINACA),

- ethyl 2-[[1-(5-fluoropentyl)indole-3-carbonyl]amino]-3,3-dimethyl-butanoate (other names: 5F-EDMB-PICA; 5F-EDMB-2201), and,
- methyl 2-(1-(4-fluorobenzyl)-1*H*-indole-3-carboxamido)-3-methyl butanoate (other name: MMB-FUBICA).

### **Posting of Public Comments**

All comments received in response to this docket are considered part of the public record. DEA will make comments available for public inspection online at <http://www.regulations.gov>, unless reasonable cause is given. Such information includes personal or business identifiers (such as name, address, state of federal identifiers, etc.) voluntarily submitted by the commenter.

Commenters submitting comments which include personal identifying information (PII), confidential, or proprietary business information that the commenter does not want to be made publicly available should submit two copies of the comment. One copy must be marked “CONTAINS CONFIDENTIAL INFORMATION” and should clearly identify all PII or business information the commenter does not want to be made publicly available, including any supplemental materials. DEA will review this copy, including the claimed PII and confidential business information, in its consideration of comments. The second copy should be marked “TO BE PUBLICLY POSTED” and must have all claimed confidential PII and business information already redacted. DEA will post only the redacted comment on <http://www.regulations.gov> for public inspection. DEA generally will not redact additional information contained in the comment marked “TO BE PUBLICLY POSTED.” The Freedom of Information Act applies to all comments received.

For easy reference, an electronic copy of this document and supplemental information to this proposed scheduling action are available at <http://www.regulations.gov>.

### **Request for Hearing or Appearance; Waiver**

Pursuant to 21 U.S.C. 811(a), this action is a formal rulemaking “on the record after opportunity for a hearing.” Such proceedings are conducted pursuant to the provisions of the

Administrative Procedure Act (APA).<sup>1</sup> Interested persons, as defined in 21 CFR 1300.01(b), may file requests for a hearing in conformity with the requirements of 21 CFR 1308.44(a) and 1316.47(a), and such requests must:

- (1) state with particularity the interest of the person in the proceeding;
- (2) state with particularity the objections or issues concerning which the person desires to be heard; and
- (3) state briefly the position of the person regarding the objections or issues.

Any interested person may file a waiver of an opportunity for a hearing or to participate in a hearing in conformity with the requirements of 21 CFR 1308.44(c), together with a written statement of position on the matters of fact and law involved in any hearing.<sup>2</sup>

All requests for a hearing and waivers of participation, together with a written statement of position on the matters of fact and law involved in such hearing, must be sent to DEA using the address information provided above. The decision whether a hearing will be needed to address such matters of fact and law in the rulemaking will be made by the Administrator. If a hearing is needed, DEA will publish a notice of hearing on the proposed rulemaking in the *Federal Register*.<sup>3</sup> Further, once the Administrator determines a hearing is needed to address such matters of fact and law in rulemaking, he will then designate an Administrative Law Judge (ALJ) to preside over the hearing. The ALJ's functions shall commence upon designation, as provided in 21 CFR 1316.52.

In accordance with 21 U.S.C. 811 and 812, the purpose of a hearing would be to determine whether 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA meet the statutory criteria for placement in schedule I, as proposed in this rulemaking.

## **Legal Authority**

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<sup>1</sup> 5 U.S.C. 551–559; 21 CFR 1308.41–1308.45; 21 CFR part 1316, subpart D.

<sup>2</sup> 21 CFR 1316.49.

<sup>3</sup> 21 CFR 1308.44(b), 1316.53.

The CSA provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General (delegated to the Administrator of DEA pursuant to 28 CFR 0.100) on her own motion, at the request of the Secretary of Health and Human Services (HHS), or on the petition of an interested party.<sup>4</sup> This proposed action is initiated on the Administrator's own motion and supported by, *inter alia*, a recommendation from the then-Assistant Secretary for Health of the HHS (Assistant Secretary) and an evaluation of all other relevant data by DEA. If finalized, this action would make permanent the existing temporary regulatory controls and administrative, civil, and criminal sanctions of schedule I controlled substances on any person who handles or proposes to handle 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA.

## **Background**

On December 12, 2023, pursuant to 21 U.S.C. 811(h)(1), the previous Administrator published an order in the *Federal Register* temporarily placing six synthetic cannabinoids (SCs) in schedule I of the CSA based on the finding that these substances pose an imminent threat to public safety.<sup>5</sup> The six SCs temporarily controlled under the CSA included the four SCs that are the subject of this proposed rulemaking, as well as methyl 3,3-dimethyl-2-(1-(pent-4-en-1-yl)-1*H*-indazole-3-carboxamido)butanoate (other name: MDMB-4en-PINACA), and 5-pentyl-2-(2-phenylpropan-2-yl)pyrido[4,3-*b*]indol-1-one (other names: CUMYL-PEGACLONE; SGT-151). These six SCs have not been investigated for medical use. Nor are they intended for human use. This proposed rulemaking focuses on 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA only.

Pursuant to 21 U.S.C. 811(b), DEA gathered the necessary data on 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA and, on April 15, 2025, submitted it

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<sup>4</sup> 21 U.S.C. 811(a).

<sup>5</sup> *Schedules of Controlled Substances: Temporary Placement of MDMB-4en-PINACA, 4F-MDMB-BUTICA, ADB-4en-PINACA, CUMYL-PEGACLONE, 5F-EDMB-PICA, and MMB-FUBICA into Schedule I*, 88 FR 86040 (Dec. 12, 2023).

to the then-Assistant Secretary for Health of HHS with a request for a scientific and medical evaluation of available information and a scheduling recommendation for 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA.

On December 3, 2025, HHS provided DEA a scientific and medical evaluation entitled, “Basis for the Recommendation to Place 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA and their salts in Schedule I of the Controlled Substances Act,” and a scheduling recommendation. Pursuant to 21 U.S.C. 811(b), following consideration of the eight factors and findings related to the substance’s abuse potential, legitimate medical use, and dependence liability, HHS recommended that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA be controlled in schedule I of the CSA under 21 U.S.C. 812(b). HHS noted that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are full agonists at the cannabinoid type 1 (CB1) receptor, have no known medical use in the United States, have no approved new drug applications, and are not known to be marketed anywhere in the world as an approved drug product. HHS also noted that health care practitioners and medical examiners have reported cases of severe clinical adverse events and even death when 4F-MDMB-BUTICA and 5F-EDMB-PICA was ingested.

### **Proposed Determination to Permanently Schedule 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA**

As discussed above in the background section, the Administrator is initiating proceedings, pursuant to 21 U.S.C. 811(a), to permanently add 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA to schedule I. DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by HHS, all other relevant data, and conducted its own eight-factor analysis in accordance with 21 U.S.C. 811(c). Included below is a brief summary of each factor as analyzed by HHS and DEA in their respective eight-factor analyses, and as considered by DEA in this proposed scheduling determination. Please note that both the DEA and HHS analyses, including the evaluation of the eight factors

determinative of control along with their supporting data and citations, are available in their entirety under the tab “Supporting Documents” of the public docket of this proposed rule at <https://www.regulations.gov>, under docket number “DEA1064.”

1. *The Drug’s Actual or Relative Potential for Abuse*

In addition to considering the information HHS provided in its scientific and medical evaluation document for 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA, DEA also considered all other relevant data regarding actual or relative potential for abuse of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA. The term “abuse” is not defined in the CSA; however, the legislative history of the CSA suggests the following four prongs in determining whether a particular drug or substances has a potential for abuse:<sup>6</sup>

- a. There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or of the community; or*
- b. There is a significant diversion of the drug or substance from legitimate drug channels; or*
- c. Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice; or*
- d. The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.*

Both DEA and HHS eight-factor analyses found that the abuse of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA is creating a hazard to the health and safety of both the individual users and others within the community. These four SCs produce pharmacological effects, including adverse effects, that are similar to those produced by other

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<sup>6</sup> Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970); reprinted in 1970 U.S.C.A.N. 4566, 4603.

schedule I SCs, such as JWH-018, FUB-AMB, and ADB-PINACA. In its letter dated March 7, 2022, HHS stated that there are no Food and Drug Administration (FDA)-approved drug products containing 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA in the United States, and there appear to be no legitimate sources for these substances as marketed drugs.

Overall, data demonstrate that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA have a high potential for abuse. Thus, based on these data, it is reasonable to conclude that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA, having no medical use, and thus no therapeutic value, present a hazard to the health and safety of individuals and the community.

## *2. Scientific Evidence of the Drug's Pharmacological Effects, if Known*

As explained in HHS's and DEA's respective eight-factor analyses, the available data indicate that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA produce pharmacological effects that are similar to those produced by schedule I SCs, such as JWH-018, FUB-AMB, and ADB-PINACA. Scientific studies demonstrate that, similar to other schedule I SCs, 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA bind to cannabinoid subtype 1 (CB1) receptors and act as agonists at CB1 receptors. Data also demonstrates that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA produce discriminative stimulus effects that are similar to SCs that have been encountered within the United States. SCs are substances synthesized in laboratories that mimic the biological effects of the schedule I hallucinogen delta-9-tetrahydrocannabinol (THC), the main psychoactive component in marijuana (schedule I). SCs were introduced to the designer drug market in several European countries as "herbal incense" before the initial encounter in the United States by U.S. Customs and Border Protection in November 2008. From 2009 to the present, misuse of SCs has increased in the United States. Law enforcement has encountered

SCs applied onto plant material and in other designer drug products intended for human consumption.

4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA have not been investigated for medical use, and they are not intended for human use. With no known legitimate use and safety information, manufacturers are surreptitiously adulterating plant material with 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and/or MMB-FUBICA, and distributors are selling the associated products which pose potentially dangerous consequences to the consumer. The adulterated products, such as “Spice,” “K2,” and many others, are marketed under the guise of “herbal incense” or “potpourri” products and as “legal alternatives to marijuana” or “legal high.” Data from law enforcement, health care practitioners, and scientific and medical literature indicate that SC products are being abused for their psychoactive properties in the absence of information regarding their safety. There have been reports of adverse effects following abuse of 4F-MDMB-BUTICA and 5F-EDMB-PICA, similar to schedule I SCs (e.g., JWH-018, FUB-AMB, and ADB-PINACA). These pharmacological characteristics of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are predictive of substances that have a high potential for abuse. Overall, these data indicate that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA produces pharmacological effects and that are similar to those of the JWH-018, FUB-AMB, and ADB-PINACA.

### *3. The State of Current Scientific Knowledge Regarding the Drug or Other Substance*

4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are structurally unrelated to THC, the principle psychoactive chemical in marijuana. Rather, 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are potent SCs that are reported to be smoked for recreational purposes. 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are CB1 receptor agonists that are pharmacologically similar to THC. Neither DEA nor HHS is aware of any currently accepted

medical use for 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA. There are no well-controlled clinical studies showing safety or efficacy for these substances. In addition, there is no evidence by qualified experts that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA are accepted as having therapeutic uses.

#### *4. History and Current Pattern of Abuse*

SCs were developed by researchers over the last 30 years as tools for investigating the endocannabinoid system. Since this first encounter, law enforcement seizures, public health and published case reports, and media reporting have demonstrated an increase in the use and abuse of SCs. Law enforcement and public health officials in the United States continue to encounter synthetic cannabinoids, including 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA. According to the National Forensic Laboratory Information System (NFLIS) data, 4F-MDMB-BUTICA was first identified in July 2020 within drug seizure evidence, which was followed by 5F-EDMB-PICA (in December 2020), 4F-MDMB-BUTICA (in February 2021), and ADB-4en-PINACA (in March 2021).<sup>7</sup> The drug seizures reported by DEA, state and local laboratories, and other federal agencies demonstrate that the four SCs are available for illicit use. In its review, HHS concluded that law enforcement data are suggestive of the illicit availability of the four SCs, which demonstrates that there is a history and current pattern of abuse of these drugs.

#### *5. Scope, Duration and Significance of Abuse*

Evidence shows that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are recreational drugs of abuse. HHS noted in its recommendation that SCs continue to be encountered on the illicit market despite scheduling actions that attempt to

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<sup>7</sup> NFLIS represents an important resource in monitoring illicit drug trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS is a comprehensive information system that includes data from forensic laboratories that handle more than 96% of an estimated 1.0 million distinct annual State and local drug analysis cases. NFLIS includes drug chemistry results from completed analyses only. While NFLIS data is not direct evidence of abuse, it can lead to an inference that a drug has been diverted and abused. *See Schedules of Controlled Substances: Placement of Carisoprodol Into Schedule IV*, 76 FR 77330, 77332 (Dec. 12, 2011).

safeguard the public from the adverse effects and safety issues associated with these substances. Novel substances continue to be encountered that differ only by small chemical structural modifications intended to avoid prosecution, while maintaining the pharmacological effects. Law enforcement and health care professionals continue to report the abuse of these substances and their associated products. According to NFLIS, there have been 568 encounters with 4F-MDMB-BUTICA, 403 encounters with ADB-4en-PINACA, 130 encounters with 5F-EDMB-PICA, and 417 encounters with MMB-FUBICA.<sup>8</sup> Despite attempts to control SCs, illicit manufacturers continue to make small chemical modifications to substances that retain pharmacological activity at the CB1 receptor; thus, they continue to be encountered on the illicit drug market. These encounters of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA by law enforcement indicate that these substances are being trafficked and abused in the United States.

#### *6. What, if Any, Risk There Is to the Public Health*

Available evidence on the overall public health risks associated with the use of SCs demonstrate that their use can cause acute health problems leading to emergency department admissions and death. Case reports detailing serious adverse effects have been reported in the literature (*see* additional details at <https://www.regulations.gov> contained within DEA's eight-factor analysis at docket DEA-1604). According to HHS, 4F-MDMB-BICA is reported to produce symptoms that are similar to other SCs. In case reports of abusers that were tested and found positive for SCs, 4F-MDMB-BICA was identified as contributing to the reported SC-like adverse symptoms. Adverse health symptoms reported from incidents involving 4F-MDMB-BICA include chest pain, respiratory problems, tremor, and seizures. Multiple deaths have also been reported following the ingestion of products containing 4F-MDMB-BICA or 5F-EDMB-PICA. While no case reports have been identified regarding ADB-4en-PINACA or MMB-

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<sup>8</sup> NFLIS data were queried on October 22, 2025.

FUBICA, due to their similar pharmacology to other schedule I SCs, it is likely that they would share a similar adverse effect profile.

*7. Its Psychic or Physiological Dependence Liability*

In its evaluation and recommendation, HHS noted that there are no clinical studies evaluating dependence liabilities specific for 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA. However, scientific data indicate that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA have a pharmacological profile that is similar to other schedule I SCs. 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA bind to the CB1 receptor, function as agonists at the CB1 receptor, and have been shown to produce discriminative stimulus effects that are similar to other schedule I SCs. Thus, it is reasonable to conclude that the cannabinoid-like properties of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA may produce a psychic and/or physiological dependence liability that is similar to other SCs already controlled in schedule I under the CSA, such as JWH-018, FUB-AMB, and ADB-PINACA.

*8. Whether the Substance is an Immediate Precursor of a Substance Already Controlled under the CSA*

4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are not immediate precursors of any substance controlled under the CSA, as defined in 21 U.S.C. 802(23).

*Conclusion:*

After considering the scientific and medical evaluation conducted by HHS, HHS's accompanying scheduling recommendation, and DEA's own eight-factor analysis, DEA finds that these facts and all relevant data constitute substantial evidence of the potential for abuse of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA. As such, DEA proposes to permanently schedule 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA as schedule I controlled substances under the CSA.

## Proposed Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as schedules I, II, III, IV, and V. The CSA also outlines the findings required to place a drug or other substance in any particular schedule.<sup>9</sup> After consideration of the analysis and recommendation of the Assistant Secretary for Health of HHS and review of all other available data, the Administrator of DEA, pursuant to 21 U.S.C. 811(a) and 812(b)(1), finds that:

(1) 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA have a high potential for abuse, evidenced in part by data from *in vitro* binding affinity and functional activity studies, as well as by data from *in vivo* drug discrimination tests in animals. In these studies, 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA were demonstrated to be agonists at CB1 receptors, which is a mechanism of action shared with other SCs substances with a high potential for abuse and controlled in schedule I under the CSA. In summary, 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA have similar patterns of drug abuse, as well as similar adverse outcomes as other SCs currently controlled in schedule I of the CSA.

(2) 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are not legally marketed in the United States, and FDA has not approved a marketing application for a drug product containing 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA for any indication. There are no known medically approved uses worldwide at this time for these substances. Moreover, there are no adequate and well-controlled clinical studies or petitioners, that claim an accepted medical use for these substances in the United States. Thus, there is no evidence that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA has a currently accepted medical use in treatment in the United States.<sup>10</sup>

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<sup>9</sup> 21 U.S.C. 812(b).

<sup>10</sup> Pursuant to 21 U.S.C 812(b)(1)(B), when placing a drug or substance in schedule I of the CSA, DEA must consider whether the substance has a currently accepted medical use in treatment in the United States. First, DEA

(3) Because 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA have no approved medical use and have not been thoroughly investigated as new drugs, their safety for use under medical supervision has not been determined. Thus, there is a lack of accepted safety for use of these substances under medical supervision.

Based on these findings, the Administrator concludes that 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA, including their salts, isomers (including optical, positional, and geometric isomers), and salts of isomers, warrant control in schedule I of the CSA.

### **Requirements for Handling 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA**

As discussed above, 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are currently subject to a temporary scheduling order, which added them to schedule I. If this rule is finalized as proposed, 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA would be subject, on a permanent basis, to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, import, export, engagement in

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looks to whether the drug or substance has FDA approval. When no FDA approval exists, DEA has traditionally applied a five-part test to a drug or substance to determine whether a drug or substance has a currently medical use: (1) the drug's chemistry must be known and reproducible; (2) there must be adequate safety studies; (3) there must be adequate and well-controlled studies proving efficacy; (4) the drug must be accepted by qualified experts; and (5) the scientific evidence must be widely available. See *Marijuana Scheduling Petition; Denial of Petition; Remand*, 57 FR 10499 (Mar. 26, 1992), pet. for rev. denied, *Alliance for Cannabis Therapeutics v. Drug Enforcement Admin.*, 15 F.3d 1131, 1135 (D.C. Cir. 1994). DEA and HHS applied the traditional five-part test for currently accepted medical use in this matter and concluded the test was not satisfied. In a recent published letter in a different context, HHS applied an additional two-part test to determine currently accepted medical use for substances that do not satisfy the five-part test: (1) whether there exists widespread, current experience with medical use of the substance by licensed health care practitioners operating in accordance with implemented jurisdiction-authorized programs, where medical use is recognized by entities that regulate the practice of medicine, and, if so, (2) whether there exists some credible scientific support for at least one of the medical conditions for which part (1) is satisfied. On April 11, 2024, the Department of Justice's Office of Legal Counsel (OLC) issued an opinion, which, among other things, concluded that HHS's two-part test would be sufficient to establish that a drug has a currently accepted medical use. Office of Legal Counsel, Memorandum for Merrick B. Garland Attorney General Re: Questions Related to the Potential Rescheduling of Marijuana at 3 (April 11, 2024). For purposes of this proposal, there is no evidence that health care providers have widespread experience with medical use of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA, or that the use of these substances is recognized by entities that regulate the practice of medicine, so the two-part test also is not satisfied.

research, conduct of instructional activities or chemical analysis with, and possession of schedule I controlled substances, including the following:

*1. Registration.* Any person who handles (manufactures, distributes, dispenses, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses) 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA must be registered with DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

*2. Security.* 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are subject to schedule I security requirements and must be handled and stored pursuant to 21 U.S.C. 821, 823, and in accordance with 21 CFR 1301.71–1301.76. Non-practitioners handling these three substances also must comply with the screening requirements of 21 CFR 1301.90–1301.93.

*3. Labeling and Packaging.* All labels and labeling for commercial containers of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA must comply with 21 U.S.C. 825 and 958(e), and be in accordance with 21 CFR part 1302.

*4. Quota.* Only registered manufacturers would be permitted to manufacture 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA in accordance with a quota assigned, pursuant to 21 U.S.C. 826, and in accordance with 21 CFR part 1303.

*5. Inventory.* Any person registered with DEA to handle 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA must have an initial inventory of all stocks of controlled substances (including these substances) on hand on the date the registrant first engages in the handling of controlled substances pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA,

and MMB-FUBICA) on hand every two years pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

*6. Records and Reports.* Every DEA registrant must maintain records and submit reports with respect to 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA, pursuant to 21 U.S.C. 827, 832(a), and 958(e), and in accordance with 21 CFR 1301.74(b) and (c) and 1301.76(b), and parts 1304, 1312, and 1317. Manufacturers and distributors would be required to submit reports regarding 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA to the Automation of Reports and Consolidated Order System pursuant 21 U.S.C. 827, and in accordance with 21 CFR parts 1304 and 1312.

*7. Order Forms.* Every DEA registrant who distributes 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA must comply with the order form requirements, pursuant to 21 U.S.C. 828 and 21 CFR part 1305.

*8. Importation and Exportation.* All importation and exportation of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

*9. Liability.* Any activity involving 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA not authorized by, or in violation of, the CSA or its implementing regulations would be unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

## **Regulatory Analyses**

### *Executive Orders 12866, 13563, 14192, and 14294*

In accordance with 21 U.S.C. 811(a), this proposed scheduling action is subject to formal rulemaking procedures done “on the record after opportunity for a hearing,” which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order (E.O.) 12866

and the principles reaffirmed in E.O.13563. DEA scheduling actions are not subject to either E.O. 14192, Unleashing Prosperity Through Deregulation, or E.O. 14294, Fighting Overcriminalization in Federal Regulations.

*Executive Order 12988, Civil Justice Reform*

This proposed regulation meets the applicable standards set forth in sections 3(a) and 3(b)(2) of E.O. 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

*Executive Order 13132, Federalism*

This proposed rulemaking does not have federalism implications warranting the application of E.O. 13132. The proposed rule does not have substantial direct effects on the States, on the relationship between the National Government and the States, or the distribution of power and responsibilities among the various levels of government.

*Executive Order 13175, Consultation and Coordination with Indian Tribal Governments*

This proposed rule does not have Tribal implications warranting the application of E.O. 13175. It does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal Government and Indian tribes, or on the distribution of power and responsibilities between the Federal Government and Indian tribes.

*Regulatory Flexibility Act*

The Administrator, in accordance with the Regulatory Flexibility Act, 5 U.S.C. 601–602, has reviewed this proposed rule and, by approving it, certifies that it will not have a significant economic impact on a substantial number of small entities.

On December 12, 2023, DEA published an order to temporarily place 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA, including their salts, isomers (including optical, positional, and geometric isomers), and salts of isomers, in schedule I of the CSA pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). DEA estimates that all entities handling or planning to handle 4F-MDMB-BUTICA, ADB-4en-

PINACA, 5F-EDMB-PICA, and MMB-FUBICA have already established and implemented systems and processes required to handle these substances. If finalized, this action would make permanent the existing regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, reverse distribute, dispense, import, export, engage in research, conduct instructional activities or chemical analysis with, or possess), or propose to handle 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA.

According to HHS, 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA have a high potential for abuse, have no currently accepted medical use in treatment in the United States, and lacks accepted safety for use under medical supervision. There appear to be no legitimate sources for 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA as marketed drug in the United States, but DEA notes that these substances are available for purchase from legitimate suppliers for scientific research. There is no evidence of significant diversion of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA from legitimate suppliers. Therefore, DEA has concluded that this proposed rule, if finalized, will not have a significant economic impact on a substantial number of small entities.

The entities affected by this proposed rule include the manufacturers, distributors, importers, exporters, and researchers of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA. DEA determines the North American Industry Classification System (NAICS) industries that best represent these business activities. Table 1 lists the business activities and corresponding NAICS industries.<sup>11</sup>

**Table 1: Business Activity and Corresponding NAICS Industries.**

<b>Business Activity</b>	<b>NAICS Code</b>	<b>NAICS Industry Description</b>
Manufacturer	325412	Pharmaceutical Preparation Manufacturing

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<sup>11</sup> Executive Office of the President Office of Management and Budget, North American Industry Classification System, United States, 2022, [https://www.census.gov/naics/reference\\_files\\_tools/2022\\_NAICS\\_Manual.pdf](https://www.census.gov/naics/reference_files_tools/2022_NAICS_Manual.pdf). (Accessed 9/25/2025).

Distributor, Importer, Exporter	424210 424690	Drugs and Druggists' Sundries Merchant Wholesalers Other Chemical and Allied Products Merchant Wholesalers
Researcher	541715  611310	Research and Development in Physical, Engineering, and Life Sciences (except Nanotechnology and Biotechnology) Colleges, Universities and Professional Schools

From Statistics of U.S. Businesses (SUSB) data, DEA determined the number of firms and small firms for each of the affected industries, and by comparing the number of affected small entities to the number of small entities for each industry, DEA determined whether a substantial number of small entities are affected in any of the industries. Table 2 lists the number of firms, small firms, and percent small firms in each affected industry.

**Table 2: Percent Affected Small Entities by Industry.**

NAICS Industry	Firms <sup>12</sup>	SBA Size Standard <sup>13</sup>	Small Firms <sup>14</sup>	Percent of Small Entities (%)
325412-Pharmaceutical Preparation Manufacturing	1,179	1,300 employees	1,099	93.2
424210-Drugs and Druggists' Sundries Merchant Wholesalers	7,012	250 employees	6,760	96.4
424690-Other Chemical and Allied Products Merchant Wholesalers	5,487	175 employees	5,197	94.7
541715-Research and Development in the Physical, Engineering, and Life Sciences (except Nanotechnology and Biotechnology)	10,042	1,000 employees	9,599	95.6
611310-Colleges, Universities and Professional Schools	2,494	\$34.5 million	1,515	60.8

Based on the American Chemical Society's SciFinder database,<sup>15</sup> DEA identified 11 entities supplying 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA across the industries 325412, 424210, and 424690. However, one entity has already registered with DEA to handle controlled substances. Hence, DEA expects only 10 of the

<sup>12</sup> Statistics of U.S. Businesses, 2022 SUSB Annual Data Tables by Establishment Industry, <https://www.census.gov/data/tables/2021/econ/susb/2021-susb-annual.html> (Accessed 9/25/2025)

<sup>13</sup> U.S. Small Business Administration, Table of size standards, Version March 2023, Effective: March 17, 2023, [https://www.sba.gov/sites/default/files/2023-06/Table%20of%20Size%20Standards\\_Effective%20March%202017%2C%202023%20%282%29.pdf](https://www.sba.gov/sites/default/files/2023-06/Table%20of%20Size%20Standards_Effective%20March%202017%2C%202023%20%282%29.pdf) (Accessed 9/25/2025)

<sup>14</sup> Based on the estimated number of firms below the SBA size standard for each industry.

<sup>15</sup> SciFinder; Chemical Abstracts Service: Columbus, OH; CAS 2504100-70-1; <https://scifinder.cas.org> (accessed September 24, 2025).

entities in the 325412, 424210, and 424690 industries will be affected by this rule. Assuming that all affected suppliers were small entities and concentrated in the smallest NAICS industry, 325412-Pharmaceutical Preparation Manufacturing, they would account for insubstantial number of small entities in that industry, 0.91 percent.<sup>16</sup>

Additionally, DEA expects that the number of researchers working with 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and/or MMB-FUBICA is small, because 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and MMB-FUBICA are not approved for medical use and have a substantial capability to be a hazard to the health of the user and to the safety of the community. Also, DEA believes that the researchers working with 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, and/or MMB-FUBICA may also work with other controlled substances; hence, these researchers are likely already registered with DEA and are qualified to handle controlled substances. For these reasons, DEA believes the number of affected researchers that are small entities is not a substantial number of small entities in 541715 and 611310 industries.

In summary, the small entities affected by this proposed rule are those in 325412-Pharmaceutical Preparation Manufacturing, 424210-Drugs and Druggists' Sundries Merchant Wholesalers, and 424690-Other Chemical and Allied Products Merchant Wholesalers. The affected small entities account for less than 0.91 percent of small businesses and are not likely to manufacture or carry inventory of 4F-MDMB-BUTICA, ADB-4en-PINACA, 5F-EDMB-PICA, or MMB-FUBICA. As such, the proposed rule, if finalized, is not expected to result in a significant economic impact on a substantial number of small entities.

#### *Unfunded Mandates Reform Act of 1995*

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1532, DEA has determined and certifies that this action would not result in any Federal mandate that may result “in the expenditure by State, local, and Tribal governments, in the aggregate, or

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<sup>16</sup> 10/1,099 = 0.91%

by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any 1 year . . . .” Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

*Paperwork Reduction Act of 1995*

This proposed rule would not impose a new collection or modify an existing collection of information under the Paperwork Reduction Act of 1995.<sup>17</sup> Also, this proposed rule would not impose new or modify existing recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. However, this proposed rule would require compliance with the following existing OMB collections: 1117-0003, 1117-0004, 1117-0006, 1117-0008, 1117-0009, 1117-0010, 1117-0012, 1117-0014, 1117-0021, 1117-0023, 1117-0029, and 1117-0056. An agency may not conduct or sponsor, and a person is not required to respond to a collection of information unless it displays a currently valid OMB control number.

**List of Subjects in 21 CFR Part 1308**

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, DEA proposes to amend 21 CFR part 1308 as follows:

**PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES**

1. The authority citation for part 1308 continues to read as follows:

**Authority:** 21 U.S.C. 811, 812, 871(b), 956(b), unless otherwise noted.

2. In § 1308.11:

- a. Add new paragraphs (d)(106-109) to read as follows;
- b. Remove and reserve paragraphs (h)(63), (64), (66) and (67):

**§ 1308.11 Schedule I.**

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(d) \* \* \*

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<sup>17</sup> 44 U.S.C. 3501–3521.

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(106) Methyl 2-[[1-(4-fluorobutyl)indole-3-carbonyl]amino]-3,3-dimethylbutanoate (other names: 4F-MDMB-BUTICA; 4F-MDMB-BICA)	7091
(107) <i>N</i> -(1-Amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(pent-4-en-1-yl)-1 <i>H</i> -indazole-3-carboxamide) (other name: ADB-4en-PINACA)	7092
(108) Ethyl 2-[[1-(5-fluoropentyl)indole-3-carbonyl]amino]-3,3-dimethylbutanoate) (other names: 5F-EDMB-PICA; 5F-EDMB-2201)	7094
(109) Methyl 2-(1-(4-fluorobenzyl)-1 <i>H</i> -indole-3-carboxamido)-3-methylbutanoate) (other name: MMB-FUBICA)	7095
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### SIGNING AUTHORITY

This document of the Drug Enforcement Administration was signed on December 10, 2025, by Administrator Terrance C. Cole. That document with the original signature and date is maintained by DEA. For administrative purposes only, and in compliance with requirements of the Office of the Federal Register, the undersigned DEA Federal Register Liaison Officer has been authorized to sign and submit the document in electronic format for publication, as an official document of DEA. This administrative process in no way alters the legal effect of this document upon publication in the Federal Register.

**Heather Achbach,**  
*Federal Register Liaison Officer,*  
*Drug Enforcement Administration.*

[FR Doc. 2025-22963 Filed: 12/15/2025 8:45 am; Publication Date: 12/16/2025]