World Health Organization

Critical Review Report:

MDMB-FUBINACA

Agenda item 3.2.1

Expert Committee on Drug Dependence

Forty-eighth Meeting

Geneva, 20-22 October 2025

This report contains the views of an international group of experts, and does not necessarily represent the decisions or the stated policy of the World Health Organization.

Contents

Executive Summary

MDMB-FUBINACA (CAS: 1971007-93-8) is a potent synthetic cannabinoid receptor agonist that is found in clandestine markets primarily in its (S)-isomer configuration. Its affinity for the CB1 receptor exceeds that of Δ^9-tetrahydrocannabinol by at least 10-fold, and it is similarly more potent at suppressing locomotor activity in mice and decreasing body temperature in rats, both of which are characteristic cannabinoid agonist effects. After smoking or vaping, MDMB-FUBINACA undergoes extensive hepatic metabolism, producing peak amounts of carboxyl acid metabolites that may be used for detection. The process of heating MDMB-FUBINACA involved in these routes of administration may also result in the formation of harmful by-products and the release of cyanide, which are subsequently inhaled. In drug discrimination studies in rodents, MDMB-FUBINACA produces Δ^9-tetrahydrocannabinol-like responding, suggesting that it would induce cannabis-like subjective effects in humans. Anecdotal evidence from online posts of people who have used MDMB-FUBINACA suggests that they do so for its intoxicating effects. Adverse effects may also occur, including agitation or sedation, nausea, short-term memory loss, tachycardia, and anxiety. MDMB-FUBINACA poisonings have resulted in numerous hospitalizations and have contributed to a minimum of 17 deaths since its first appearance on the illicit market in 2014 in the Federation of Russia. Since then, MDMB-FUBINACA has been detected in at least nineteen countries. While national drug control regulations enacted from 2015 to 2020 were successful in decreasing the prevalence of MDMB-FUBINACA detections, a novel one-step synthesis process wherein MDMB-FUBINACA and other controlled synthetic cannabinoid receptor agonists are synthesized from precursor compounds has resulted in a recent uptick in encounters with MDMB-FUBINACA. This process allows the synthesis of MDMB-FUBINACA in local clandestine laboratories from which it can be distributed with less risk of detection.

1. Substance identification

A. International Nonproprietary Name (INN)

Not assigned

B. Chemical Abstracts Service (CAS) Registry Number

1971007-93-8

C. Other chemical names

MDMB-FUBINACA
MDMB-Fubinaca
N-[[1-[(4-Fluorophenyl)methyl]-1*H*-indazol-3-yl]carbonyl]-3-methyl-L-valine methyl ester (ACI)

D. Trade names

Not assigned

E. Street names

No specific information is available on the street names of MDMB-FUBINACA, but it might be found under its own name.

F. Physical appearance

MDMB-FUBINACA has been found sprayed onto herbal products, similar to other synthetic cannabinoids (SCs) that have been previously encountered (Drug Enforcement Administration, 2019; Lee et al., 2017). SCs are generally marketed as dried leaves or powder. The leaves come in packages with appealing designs in which the product is sprayed with one or more SC types. When found as a powder, it is usually white, but it has also been found in other colors and can be dissolved in either ethanol or acetone. (Papaseit et al., 2018).
As a reference material, MDMB-FUBINACA is sold as a neat solid and has a characteristic odor, though it has not been specified (Cayman Chemical, 2025).

2. Chemistry

A. Chemical name

IUPAC name:
Methyl 2-{[1-(4-fluorobenzyl)indazole-3-carbonyl]amino}-3,3-dimethylbutanoate

CA Index name:
Not assigned

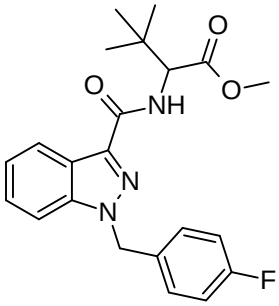
Canonical SMILES:
O=C(OC)C(NC(=O)C1=NN(C=2C=CC=CC12)CC3=CC=C(F)C=C3)C(C)(C)C

InChI:
InChI=1S/C22H24FN3O3/c1-22(2,3)19(21(28)29-4)24-20(27)18-16-7-5-6-8-17(16)26(25-18)13-14-9-11-15(23)12-10-14/h5-12,19H,13H2,1-4H3,(H,24,27)/t19-/m1/s1

InChI key:
RFCDVEHNYDVCMU-LJQANCHMSA-N

B. *Chemical structure*

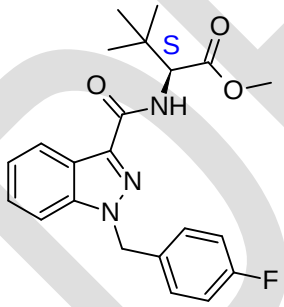
Free base:



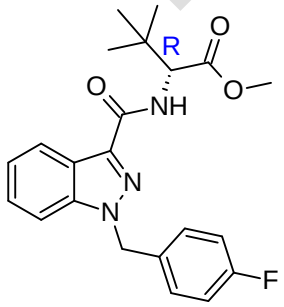
Molecular formula: $C_{22}H_{24}FN_3O_3$
Molecular weight: 397.44 g/mol

C. *Stereoisomers*

MDMB-FUBINACA presents one stereogenic centre (C2), therefore it can exist as two stereoisomers (enantiomers): Methyl (2*S*)-2-{[1-(4-fluorobenzyl)indazole-3-carbonyl]amino}-3,3-dimethylbutanoate and methyl (2*R*)-2-{[1-(4-fluorobenzyl)indazole-3-carbonyl]amino}-3,3-dimethylbutanoate.



Methyl (2*S*)-2-{[1-(4-fluorobenzyl)indazole-3-carbonyl]amino}-3,3-dimethylbutanoate



Methyl (2*R*)-2-{[1-(4-fluorobenzyl)indazole-3-carbonyl]amino}-3,3-dimethylbutanoate

Historically, structurally related synthetic cannabinoid receptor agonists (SCRAs) featuring such chiral centres have typically shown the (*S*)-configuration. (Gioé-Gallo et al., 2023). It is likely that the MDMB-FUBINACA circulating on the market is found with the absolute (*S*)-configuration, although the presence of the other enantiomer cannot be excluded either as a single isomeric form or as an impurity (Doi et al., 2016).

D. Methods and ease of illicit manufacture

No specific information about the methods and ease of illicit manufacture of the MDMB-FUBINACA products circulating on the drug market was found. However, some synthetic procedures are reported in the literature, and all involve similar reagents and conditions. A very common reported procedure is based on the original patent by Buchler et al. (Buchler et al., 2009) and starts with the commercially available methyl indazole 3-carboxylate, which is reacted under basic conditions (t-BuOH in THF at 0 °C) with 1-(bromomethyl)-4-fluorobenzene to give the corresponding N1-alkylated indazole in a regioselective manner. The latter undergoes saponification with 1 M aqueous NaOH (sodium hydroxide) in refluxing MeOH (methanol) for 24 h, yielding the corresponding acid. The final product MDMB-FUBINACA is finally obtained by coupling the acid with methyl L-valinate and adding EDC·HCl [1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride], HOBt (N-hydroxybenzotriazole), and DIPEA (N,N-diisopropylethylamine) in DMSO (dimethylsulfoxide) at room temperature (Banister et al., 2016; Antonides et al., 2021; Brandon et al., 2021).

The synthesis of MDMB-FUBINACA is not regarded as particularly complex, as it follows a straightforward multistep sequence starting from unregulated commercially available precursors. The main transformations—N1-alkylation, ester hydrolysis, and amide coupling—are standard reactions in synthetic organic chemistry and rely on commonly available reagents and conditions. The overall procedure is well established in the literature and can be reproduced without specialized equipment.

Following restriction measures enacted from 2015 to 2020 to decrease the SCRAs' illicit market, a new one-step synthesis process was adopted to obtain MDMB-FUBINACA and other illegal SCRAs from precursor compounds lacking the tail moiety typical of most synthetic cannabinoids (e.g., the 4-fluoromethyl substituent in the case of MDMB-FUBINACA) (Monti et al., 2025). This simplified synthetic procedure allows the online purchase of non-banned tail-less precursors as part of “Do-It-Yourself (DIY) kits”, which also include necessary reagents and step-by-step instructions on how to obtain the desired SCRA.

E. Chemical properties

Melting-point:
No information was found

Boiling-point:
No information was found

Solubility (Cayman Chemical, 2019)*:*

- DMF: 15 mg/mL
- DMF: PBS (pH 7.2) (1:3): 0.25 mg/mL
- DMSO: 2 mg/mL
- Ethanol: 2 mg/ml

F. Identification and analysis

Reference material

A GC-MS method was employed to analyse the pyrolysis products of six carboxamide-type synthetic cannabinoids, including MDMB-FUBINACA, which resulted in degradation above 600 °C into 1-(4-fluorobenzyl)-1H-indazole, 1-(4-fluorobenzyl)-1H-indazole-3-carbonitrile, 1-(4-fluorobenzyl)-1H-indazole-3-carboxamide, and 1-(4-fluorobenzyl)-N-neopentyl-1H-indazole-3-carboxamide. Generation of potentially toxic compounds, including naphthalene, 1-naphthylamine, and toluene, as well as the release of cyanide, was observed at temperatures above 400 °C (Kevin et al., 2019).

The pure reference material was also recently characterized via LC-HRMS with the Orbitrap technology, which allowed for a complete characterization of the higher collisional dissociation (HCD) profile, including all of its fragment ion structures (Selwe et al., 2025).

Seized material

M. R. Peace et al. investigated the chemical composition of three e-liquids for electronic cigarettes by gas chromatography with flame ionization detector (HS-GC-FID). Solid phase micro-extraction gas chromatography mass spectrometry (SPME-GC-MS) was also used to analyze the aerosol produced from the e-liquids after vaporization through an e-cigarette. MDMB-FUBINACA was determined to be the major active ingredient in all samples (Peace et al., 2017).

In 2020, N. S. Kim et al. developed an LC-QToF/MS method and validated an LC-MS/MS method for the simultaneous quantification of 14 NPS, including MDMB-FUBINACA, which was determined with a LOD of 0.02 ng/mL and a LOQ of 0.06 ng/mL in both solid and liquid matrices. The method was applied to 65 different matrix samples, including capsules, tablets, powders, pills, and tea leaves, although MDMB-FUBINACA was not detected. The substance was also characterized via 1H and 13C NMR (Kim et al., 2021).

Biological samples

P. Kavanagh et al. identified MDMB-FUBINACA metabolites in six urine samples collected from patients admitted to hospital with suspected drug intoxications and from postmortem forensic investigations by LC-QToF. Hydrolysis of the terminal methyl ester groups was the first transformation encountered, followed by monohydroxylation, dihydrodiol formation, fluorobenzyl loss, and dehydrogenation. All these metabolites were also detected in the forms of glucuronides. Two unhydrolyzed metabolites were identified as products of

hydroxylation and fluorobenzyl loss with subsequent glucuronidation. However, no quantification of the parent compound was reported (Kavanagh et al., 2017).

A. Al-Matrouk et al. reviewed and analyzed 510 cases from three different forensic laboratories in Kuwait in 2018. Plant material and dried leaves were analysed under a stereomicroscope. All samples were analysed by GC-MS, and urine samples were also analysed by LC-HRMS/MS and ELISA. MDMB-FUBINACA was detected in one urine sample in combination with other SCs (Al-Matrouk et al., 2019).

R. S. Ong et al. validated an LC-MS/MS (QqQ) method for the simultaneous analysis of 29 SCs, including MDMB-FUBINACA and metabolites, 4 amphetamines, and 2 cannabinoids in human whole blood. The limit of detection (LOD) and the limit of confirmation (LOC) were both 1 ng/mL. The method was applied to the analysis of 564 ante- and post-mortem blood samples in 2018, but the substance was found in only 8 cases, as the corresponding acid at concentrations below 10 ng/mL rather than in unchanged form (Ong et al., 2020).

Supported liquid extraction and LC-QToF with All Ions data acquisition were used to determine the concentrations of MDMB-FUBINACA in whole blood, with LOQ and LOD of 2 and 1 ng/mL, respectively (Ayala and Kerrigan, 2023).

S. Chen et al. developed and validated a UHPLC-MS/MS method for the determination of five SCs, including MDMB-FUBINACA, in wastewaters samples after extraction with poly (methacrylic acid-co-ethylene glycol dimethacrylate)- functionalized polydopamine-coated Fe3O4 nanoparticles and pre-concentration with magnetic solid-phase extraction (MSPE). The method showed a LOQ of 0.1 ng/L. However, the substance was not detected in any of the 23 wastewater samples collected from China (Chen et al., 2023).

3. Ease of conversion into controlled substances

The molecule of MDMB-FUBINACA presents an amide bond, which can be easily hydrolysed under acidic conditions (strong acid and high temperature). Such conditions do not affect the indazole ring, but likely only the terminal methyl ester. Once the amide bond is broken, the acid may be conjugated to another amino acid like L-valine, as in AB-FUBINACA (Schedule II of the 1971 Single Convention on Psychotropic Substances since 2020).

By breaking both the terminal ester bond and the bond between the indazole nitrogen and the benzyl carbon, other compounds can be obtained, such as ADB-FUBINACA (Schedule II of the 1971 Single Convention on Psychotropic Substances since 2019).

4. General Pharmacology

A. Routes of administration and dosage

Posts on online forums by people who use drugs indicate that MDMB-FUBINACA is inhaled by smoking and by vaping after solubilization (Reddit, 2025). Smoking and vaping as routes of administration are also suggested by the analytically confirmed presence of MDMB-FUBINACA in plant material that has been sprayed with the substance (Welsh

Emerging Drugs and Identification of Novel Substances Project, 2025; Drug Enforcement Administration, 2019), and in commercially available e-liquids for use in electronic cigarette devices (Peace et al., 2017). In some of these cases, MDMB-FUBINACA was the sole substance identified in tested samples.

The dosage required for intoxication is unclear. Posts on online forums by people who use drugs suggest that doses in the microgram range (< 25 μg) are optimal, as higher doses "… sent my mind and body someplace else" (Reddit, 2025). These online forum posts should be considered anecdotal, as there was no analytical confirmation of the presence or purity of MDMB-FUBINACA.

B. Pharmacokinetics

Like many synthetic cannabinoids, MDMB-FUBINACA undergoes extensive hepatic biotransformation in the body. Analysis of the metabolites of urine samples collected post-mortem and from intoxicated individuals admitted to the hospital revealed twenty-two metabolites, many of which were also formed by metabolism of a closely related analog, ADB-FUBINACA (i.e., amide group is substituted for the methyl ester of MDMB-FUBINACA) (Kavanagh et al., 2017). Hydrolysis of the methyl ester resulted in several high-yield metabolites with terminal carboxyl groups. Other Phase I metabolic processes included hydroxylation, dehydrogenation, dihydrodiol formation, and loss of the fluorobenzyl substituent. Phase II glucuronidation produced additional metabolites. The recommended strategy for detection in urine was to screen for carboxyl acid metabolites because of their abundance followed by confirmation with screening for hydroxylated metabolites, especially the metabolite formed by ester hydrolysis and hydroxylation at the neopentane group. This latter metabolite is suggested because of its relatively minor alteration from the parent compound.

The distribution and clearance of MDMB-FUBINACA were investigated in a second in vitro pharmacokinetics study (Brandon et al., 2021). Results showed that the active *S*-isomer of MDMB-FUBINACA was highly protein-bound (99.5%) and exhibited plasma stability of 91.6-94.2% after incubation for 5 h. In vitro half-life ($t_{1/2}$) in pooled human hepatocytes was 11 min for the *S*-isomer and 20 min for the *R*-isomer. The predicted human in vivo hepatic clearance rate for *(S)*-MDMB-FUBINACA was estimated at 1.39 mL min^{-1} kg^{-1}.

C. Pharmacodynamics

MDMB-FUBINACA binds to both human type 1 cannabinoid (hCB1) and hCB2 receptors, with high affinities at both cannabinoid receptors: hCB1 Ki = 0.10 nM (± standard error of the mean: 0.03 nM) (Schoeder et al., 2018) and 1.14 nM (95% confidence interval: 0.87; 1.50 nM) (Gamage et al., 2018) and hCB2 Ki = 0.13 (± standard error of the mean: 0.01 nM) (Schoeder et al., 2018) and 0.12 nM (95% confidence interval: 0.09; 0.16 nM) (Gamage et al., 2018). For comparison purposes, the affinities for Δ^9-tetrahydrocannabinol at hCB1 receptors were 3.87 nM (Schoeder et al., 2018) and 16.17 nM (Gamage et al., 2018). Binding models further confirm binding of MDMB-FUBINACA to the CB1 receptor and elucidate its specific binding loci and mechanisms within the receptor (Krishna Kumar et al., 2019; Liao et al., 2023; Rangari et al., 2025).

MDMB-FUBINACA showed functional activation of both cannabinoid receptors in several assays. It stimulated [^{35}S]GTPγS at both CB1 and CB2 receptors: half maximal effective concentration (EC50) = 0.27 nM and 0.14 nM, respectively (Gamage et al., 2018). Further, it inhibited forskolin-stimulated cyclic adenosine monophosphate (cAMP) production at both receptors, with EC50s ranging from 0.06 to 0.66 nM for CB1 receptors (Gamage et al., 2018; Schoeder et al., 2018) and EC50 = 0.76 nM for CB2 receptors (Schoeder et al., 2018). MDMB-FUBINACA also was a full, potent agonist at both cannabinoid receptors in a fluorescence-based membrane assay in AtT20 cells, with greater potency for activation of CB1 than of CB2 receptors: EC50 = 3.9 nM, Emax = 108% (compared with CP55,940) for the CB1 receptor and EC50 = 55 nM, Emax = 101% (compared with CP55,940) for the CB2 receptor (Banister et al., 2016).

In vivo, MDMB-FUBINACA dose dependently suppressed locomotor activity in mice (ED50 = 0.04 mg/kg) (Gatch and Forster, 2019). The onset of this effect occurred at 10-20 min, with a duration of 120-440 min at the peak dose of 0.1 mg/kg. By comparison, Δ^9-tetrahydrocannabinol was less potent (ED50 = 7.9 mg/kg), but its effect was of similar duration (120-340 min). In rats, MDMB-FUBINACA induced hypothermia at doses ranging from 0.01 to 1 mg/kg (Banister et al., 2016). This effect was long-lasting, as body temperature did not return to normal until 8 h after treatment, and was reversible by the CB1 receptor antagonist rimonabant, but not by the CB2 receptor antagonist SR144528. In the same rats, MDMB-FUBINACA produced mild bradycardia.

A single in vitro study examined the effects of MDMB-FUBINACA on brain angiogenesis (Al-Eitan and Alkhawaldeh, 2023). This study found that MDMB-FUBINACA promoted angiogenesis in human brain microvascular endothelial cells without affecting their viability. Concomitant increases in pro-angiogenic factors (angiopoietins 1 and 2 and vascular endothelial growth factor) were observed. While these results could suggest that MDMB-FUBINACA might be useful for conditions in which angiogenesis is disrupted, further research would be needed.

5. Toxicology

No information was found on the toxicology of MDMB-FUBINACA.

6. Adverse Reactions in Humans

MDMB-FUBINACA has been associated with various adverse reactions in humans, including death. In 2014, Russian authorities reported over 600 poisonings and 15 deaths resulting from the use of MDMB-FUBINACA during a two-week period (European Monitoring Centre for Drugs and Drug Addiction, 2017; European Monitoring Centre for Drugs and Drug Addiction, 2015). Two deaths associated with MDMB-FUBINACA were reported in Europe and in the US (Drug Enforcement Agency, 2017; United Nations Office on Drugs and Crime, 2025b). Although details about the deaths were not noted, high causality was attributed to MDMB-FUBINACA in the US death. Reported symptoms of analytically confirmed MDMB-FUBINACA ingestion include agitation or sedation, vomiting, short-term memory loss, salivation, rhinorrhea, mydriasis, tachycardia, and anxiety (Kavanagh et al., 2017; Drug Enforcement Agency, 2017).

Posts on online forums by people who use drugs suggest that MDMB-FUBINACA is potent, with altered consciousness occurring at higher doses (i.e., mg vs. μg) (Reddit, 2025). These online forum posts should be considered anecdotal, as there was no analytical confirmation of the purity of MDMB-FUBINACA.

7. Dependence Potential

A. Animal Studies

No information was found.

B. Human Studies

No information was found.

8. Abuse Potential

A. Animal Studies

Drug discrimination is a pharmacologically selective animal model of the subjective effects of psychoactive drugs in humans. MDMB-FUBINACA has been assessed in drug discrimination in both mice and rats. Adult male C57/Bl6J mice were trained to discriminate Δ^9-tetrahydrocannabinol (5.6 mg/kg intraperitoneally) from vehicle using a two nose-poke procedure for food reward. MDMB-FUBINACA produced a dose-dependent switch from responding on the vehicle-associated nose-poke to responding on the Δ^9-tetrahydrocannabinol-associated nose-poke, with an ED50 of 0.02 mg/kg (95% confidence interval: 0.01; 0.04 mg/kg) (Gamage et al., 2018). In Sprague-Dawley rats trained to discriminate Δ^9-tetrahydrocannabinol (3 mg/kg intraperitoneally) from vehicle in a standard two-lever procedure with food reinforcement, MDMB-FUBINACA produced full dose-dependent substitution for the Δ^9-tetrahydrocannabinol training dose, with an ED50 of 0.051 mg/kg (± standard error of the mean: 0.013 mg/kg) (Gatch and Forster, 2019). These results suggest that MDMB-FUBINACA has subjective effects in humans similar to those of Δ^9-tetrahydrocannabinol.

B. Human Studies

No information was found.

9. Therapeutic Applications and Extent of Therapeutic Use and Epidemiology of Medical Use

There are no known therapeutic uses for MDMB-FUBINACA.

10. Listing on the WHO Model List of Essential Medicines

MDMB-FUBINACA is not listed on the 23rd WHO Model List of Essential Medicines or on the 9th WHO Model List of Essential Medicines for Children.

11. Marketing Authorizations (as a Medicinal Product)

MDMB-FUBINACA has no known marketing authorizations.

12. Industrial Use

MDMB-FUBINACA has no known industrial use.

13. Non-Medical Use, Abuse, and Dependence

MDMB-FUBINACA first appeared on the illicit market in 2014 in the Russian Federation, where it was associated with a cluster of overdoses and deaths (European Monitoring Centre for Drugs and Drug Addiction, 2015). From there, its use spread to other countries. Reports on online forums by people who use drugs provide evidence that MDMB-FUBINACA has been used intentionally for its intoxicating effects (see section 6). To date, the presence of this substance has been reported in at least nineteen countries (see section 16 for listing). The prevalence of chronic use and dependence of MDMB-FUBINACA has not been reported.

14. Nature and Magnitude of Public Health Problems Related to Misuse, Abuse, and Dependence

MDMB-FUBINACA use has been associated with mortality and morbidity in several countries. Deaths from analytically confirmed use of MDMB-FUBINACA have occurred in the Russian Federation (n=15) and in the US (n=1) (Kavanagh et al., 2017; United Nations Office on Drugs and Crime, 2025b). The cause of death in these cases was attributed to MDMB-FUBINACA with high probability. MDMB-FUBINACA was also associated with numerous hospitalizations in these countries. Information on the specific effects of MDMB-FUBINACA on driving was not identified. MDMB-FUBINACA has infiltrated prisons in Scotland and in the US, where it was used by inmates (Monti et al., 2025; Hvozdovich et al., 2020), resulting in 2 overdoses in a prison in the US state of Florida (Hvozdovich et al., 2020). MDMB-FUBINACA was detected in samples of e-liquids that were commercially available for use in electronic cigarettes and for which the chemical content was not advertised (Peace et al., 2017). MDMB-FUBINACA was the primary psychoactive ingredient in these products.

15. Licit Production, Consumption, and International Trade

No information was found.

16. Illicit Manufacture and Traffic and Related Information

MDMB-FUBINACA first appeared on the illicit market in the Federation of Russia in 2014 (European Monitoring Centre for Drugs and Drug Addiction, 2015). By 2016, its presence in European countries triggered a public health alert from the EMCDDA (European Monitoring Centre for Drugs and Drug Addiction, 2017). By 2017, MDMB-FUBINACA had spread to the US and was of sufficient concern that authorities issued its temporary placement in Schedule 1 of the US Controlled Substances Act (Drug Enforcement Agency, 2017). The National Forensic Laboratory Information System (NFLIS) in the US reported 507 encounters specifically with MDMB-FUBINACA in twenty-two states

from 2015-2016 (Drug Enforcement Agency, 2017). The NFLIS database contains cases in which a substance was analyzed as part of an investigation of drug trafficking, distribution, or abuse.

Search of the database maintained by the United Nations Office on Drugs and Crime, Early Warning Advisory on Novel Psychoactive Substances (United Nations Office on Drugs and Crime, 2025a) revealed numerous countries in which the presence of MDMB-FUBINACA has been reported, including Austria, China, Czechia, France, Germany, Hungary, Ireland, Kazakhstan, Kyrgyzstan, Latvia, the Russian Federation, Republic of Türkiye, the United States, Uzbekistan, and Vietnam. Other countries in which MDMB-FUBINACA has been detected include Korea (United Nations Office on Drugs and Crime, 2025b), Kuwait (Al-Matrouk et al., 2019), New Zealand (Ong et al., 2020), and the United Kingdom (Welsh Emerging Drugs and Identification of Novel Substances Project, 2025).

National regulations controlling MDMB-FUBINACA (see Section 18), especially in China, dramatically decreased detections by 2018 (Monti et al., 2025). However, the number of detections by forensic agencies has increased recently. For example, in the second quarter of 2025, samples from two toxicology cases showed the presence of MDMB-FUBINACA (Center for Forensic Science Research and Education, 2025). This increase is thought to be the result of a new one-step synthesis process wherein MDMB-FUBINACA and other illegal synthetic cannabinoids are synthesized from precursor compounds that lack the tail moiety typical of most synthetic cannabinoids (e.g., the 4-fluoromethyl substituent of MDMB-FUBINACA) (Monti et al., 2025). Further, the synthesis process has been considerably simplified. Hence, non-banned tail-less precursors can be purchased online and used to synthesize MDMB-FUBINACA in local clandestine laboratories, which in turn, has facilitated distribution.

17. Current International Controls and Their Impact

MDMB-FUBINACA has not been previously reviewed by WHO and is not currently under international control.

18. Current and Past National Controls

MDMB-FUBINACA is classified as a Schedule 1 drug in the US (Drug Enforcement Administration, 2020). It is also illegal in the Federation of Russia, China, and most of the EU (Monti et al., 2025).

19. Other Medical and Scientific Matters Relevant for a Recommendation on the Scheduling of the Substance

Because the most common routes of administration for MDMB-FUBINACA are smoking and vaping, people using this substance may be exposed to thermal degradants of the parent compound. Kevin et al (Kevin et al., 2019) delineated the degradants formed when the parent compound was heated to high temperatures (200-800^{o}C). They also reported the release of 27.44 μg cyanide following exposure of 1 mg MDMB-FUBINACA to a temperature of 800 °C. These results suggest that the route of administration is an

important consideration when determining the potential net consequences of MDMB-FUBINACA use.

References

AL-EITAN, L. & ALKHAWALDEH, M. 2023. MDMB-FUBINACA Influences Brain Angiogenesis and the Expression of VEGF, ANG-1, and ANG-2. *Curr Vasc Pharmacol,* 21**,** 356-365.

AL-MATROUK, A., ALQALLAF, M., ALSHEMMERI, A. & BOJBARAH, H. 2019. Identification of synthetic cannabinoids that were seized, consumed, or associated with deaths in Kuwait in 2018 using GC-MS and LC-MS-MS analysis. *Forensic Sci Int,* 303**,** 109960.

ANTONIDES, L. H., CANNAERT, A., NORMAN, C., NICDÁEID, N., SUTCLIFFE, O. B., STOVE, C. P. & MCKENZIE, C. 2021. Shape matters: The application of activity-based in vitro bioassays and chiral profiling to the pharmacological evaluation of synthetic cannabinoid receptor agonists in drug-infused papers seized in prisons. *Drug Test Anal,* 13**,** 628-643.

AYALA, J. & KERRIGAN, S. 2023. Comprehensive toxicological screening of common drugs of abuse, new psychoactive substances and cannabinoids in blood using supported liquid extraction and liquid chromatography-quadrupole time-of-flight mass spectrometry. *J Anal Toxicol,* 47**,** 656-667.

BANISTER, S. D., LONGWORTH, M., KEVIN, R., SACHDEV, S., SANTIAGO, M., STUART, J., MACK, J. B., GLASS, M., MCGREGOR, I. S., CONNOR, M. & KASSIOU, M. 2016. Pharmacology of valinate and tert-leucinate synthetic cannabinoids 5F-AMBICA, 5F-AMB, 5F-ADB, AMB-FUBINACA, MDMB-FUBINACA, MDMB-CHMICA, and their analogues. *ACS Chem Neurosci,* 7**,** 1241-54.

BRANDON, A. M., ANTONIDES, L. H., RILEY, J., EPEMOLU, O., MCKEOWN, D. A., READ, K. D. & MCKENZIE, C. 2021. A Systematic Study of the In Vitro Pharmacokinetics and Estimated Human In Vivo Clearance of Indole and Indazole-3-Carboxamide Synthetic Cannabinoid Receptor Agonists Detected on the Illicit Drug Market. *Molecules,* 26**,** 1396.

BUCHLER, I. P., HAYES, M. J., HEDGE, S. G., HOCKERMAN, S. L., KORTUM, S. W., RICO, J. G., TENBRINK, R. E. & WU, K. K. 2009. *Indazole derivatives. WO2009106982A1*.

CAYMAN CHEMICAL. 2025. *MDMB-FUBINACA* [Online]. Available at: https://www.caymanchem.com/product/16966/mdmb-fubinaca?srsltid=AfmBOorL9i8xQuDft4jf8Gu86G4vkbG1Uq_B2pdzcLqTJPJigfaaRlk6. [Accessed July 5 2025].

CENTER FOR FORENSIC SCIENCE RESEARCH AND EDUCATION. 2025. *Quarterly trend reports for synthetic cannabinoids* [Online]. Available at: https://www.cfsre.org/images/trendreports/2025-Q2-Synthetic-Cannabinoids-Trend-Report.pdf. [Accessed August 15 2025].

CHEN, S., QIE, Y., HUA, Z., ZHANG, H., WANG, Y., DI, B. & SU, M. 2023. Preparation of poly(methacrylic acid-co-ethylene glycol dimethacrylate)-functionalized magnetic polydopamine nanoparticles for the extraction of six cannabinoids in wastewater followed by UHPLC-MS/MS. *Talanta,* 264**,** 124752.

DOI, T., ASADA, A., TAKEDA, A., TAGAMI, T., KATAGI, M., KAMATA, H. & SAWABE, Y. 2016. Enantioseparation of the carboxamide-type synthetic cannabinoids N-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(5-fluoropentyl)-1H-indazole-3-carboxamide and methyl [1-(5-fluoropentyl)-1H-indazole-3-carbonyl]-valinate in illicit herbal products. *J Chromatogr A,* 1473**,** 83-89.

DRUG ENFORCEMENT ADMINISTRATION 2019. Schedules of Controlled Substances: Placement of 5F–ADB, 5F–AMB, 5F–APINACA, ADB–FUBINACA, MDMB–CHMICA and MDMB–FUBINACA in Schedule 1. Fed Regist, 84, 13848-13853.

DRUG ENFORCEMENT ADMINISTRATION 2020. Schedules of Controlled Substances: Placement of 5F-ADB, 5F-AMB, 5FAPINACA, ADB-FUBINACA, MDMBCHMICA and MDMB-FUBINACA in Schedule I. *Fed Regist,* 85**,** 4211-4215.

DRUG ENFORCEMENT AGENCY 2017. Schedules of controlled substances: Temporary placement of six synthetic cannabinoids (5F-ADB, 5F-AMB, 5F-APINACA, ADB-FUBINACA, MDMB-CHMICA and MDMB-FUBINACA) into Schedule I. Federal Register.

EUROPEAN MONITORING CENTRE FOR DRUGS AND DRUG ADDICTION 2015. EMCDDA–Europol 2014 Annual Report on the implementation of Council Decision 2005/387/JHA, Implementation reports. Luxembourg: Publications Office of the European Union.

EUROPEAN MONITORING CENTRE FOR DRUGS AND DRUG ADDICTION. 2017. *Synthetic cannabinoids in Europe (Perspectives on drugs)* [Online]. Lisbon: Available at: https://www.euda.europa.eu/publications/pods/synthetic-cannabinoids_en. [Accessed August 15 2025].

GAMAGE, T. F., FARQUHAR, C. E., LEFEVER, T. W., MARUSICH, J. A., KEVIN, R. C., MCGREGOR, I. S., WILEY, J. L. & THOMAS, B. F. 2018. Molecular and behavioral pharmacological characterization of abused synthetic cannabinoids MMB- and MDMB-FUBINACA, MN-18, NNEI, CUMYL-PICA, and 5-Fluoro-CUMYL-PICA. *J Pharmacol Exp Ther,* 365**,** 437-446.

GATCH, M. B. & FORSTER, M. J. 2019. Cannabinoid-like effects of five novel carboxamide synthetic cannabinoids. *Neurotoxicology,* 70**,** 72-79.

GIOÉ-GALLO, C., ORTIGUEIRA, S., BREA, J., RAÏCH, I., AZUAJE, J., PALEO, M. R., MAJELLARO, M., LOZA, M. I., SALAS, C. O., GARCÍA-MERA, X., NAVARRO, G. & SOTELO, E. 2023. Pharmacological insights emerging from the characterization of a large collection of synthetic cannabinoid receptor agonists designer drugs. *Biomed Pharmacother,* 164**,** 114934.

HVOZDOVICH, J. A., CHRONISTER, C. W., LOGAN, B. K. & GOLDBERGER, B. A. 2020. Case Report: Synthetic Cannabinoid Deaths in State of Florida Prisoners. *J Anal Toxicol,* 44**,** 298-300.

KAVANAGH, P., GRIGORYEV, A. & KRUPINA, N. 2017. Detection of metabolites of two synthetic cannabimimetics, MDMB-FUBINACA and ADB-FUBINACA, in authentic human urine specimens by accurate mass LC–MS: a comparison of intersecting metabolic patterns. *Forensic Toxicology,* 35**,** 284-300.

KEVIN, R. C., KOVACH, A. L., LEFEVER, T. W., GAMAGE, T. F., WILEY, J. L., MCGREGOR, I. S. & THOMAS, B. F. 2019. Toxic by design? Formation of thermal degradants and cyanide from carboxamide-type synthetic cannabinoids CUMYL-PICA, 5F-CUMYL-PICA, AMB-FUBINACA, MDMB-FUBINACA, NNEI, and MN-18 during exposure to high temperatures. *Forensic Toxicol,* 37**,** 17-26.

KIM, N. S., LIM, N. Y., CHOI, H. S., LEE, J. H., KIM, H. & BAEK, S. Y. 2021. Application of a simultaneous screening method for the detection of new psychoactive substances in various matrix samples using liquid chromatography/electrospray ionization tandem mass spectrometry and liquid chromatography/quadrupole time-of-flight mass spectrometry. *Rapid Commun Mass Spectrom,* 35**,** e9067.

KRISHNA KUMAR, K., SHALEV-BENAMI, M., ROBERTSON, M. J., HU, H., BANISTER, S. D., HOLLINGSWORTH, S. A., LATORRACA, N. R., KATO, H. E., HILGER, D., MAEDA, S., WEIS, W. I.,

FARRENS, D. L., DROR, R. O., MALHOTRA, S. V., KOBILKA, B. K. & SKINIOTIS, G. 2019. Structure of a Signaling Cannabinoid Receptor 1-G Protein Complex. *Cell,* 176**,** 448-458.e12.

LEE, J. H., PARK, H. N., LEEM, T.-S., JEON, J.-H., CHO, S., LEE, J. & BAEK, S. Y. 2017. Identification of new synthetic cannabinoid analogue APINAC (adamantan-1-yl 1-pentyl-1H-indazole-3-carboxylate) with other synthetic cannabinoid MDMB(N)-Bz-F in illegal products. *Forensic Toxicology,* 35**,** 45-55.

LIAO, Y. Y., ZHANG, H., SHEN, Q., CAI, C., DING, Y., SHEN, D. D., GUO, J., QIN, J., DONG, Y., ZHANG, Y. & LI, X. M. 2023. Snapshot of the cannabinoid receptor 1-arrestin complex unravels the biased signaling mechanism. *Cell,* 186**,** 5784-5797.e17.

MONTI, M. C., RAUTIO, T., DEVENTER, M. H., SCHLÄPFER, M., TVEIT, J., KROTULSKI, A. J., MARLAND, V., REID, R., DAEID, N. N., MCKENZIE, C., STOVE, C. P., GREEN, H. & NORMAN, C. 2025. Tail-less precursors in synthetic cannabinoid production: investigating a clandestine laboratory, seized samples, and CB1 activity. *Archives of Toxicology*.

ONG, R. S., KAPPATOS, D. C., RUSSELL, S. G. G., POULSEN, H. A., BANISTER, S. D., GERONA, R. R., GLASS, M., JOHNSON, C. S. & MCCARTHY, M. J. 2020. Simultaneous analysis of 29 synthetic cannabinoids and metabolites, amphetamines, and cannabinoids in human whole blood by liquid chromatography-tandem mass spectrometry - A New Zealand perspective of use in 2018. *Drug Test Anal,* 12**,** 195-214.

PAPASEIT, E., PÉREZ-MAÑÁ, C., PÉREZ-ACEVEDO, A. P., HLADUN, O., TORRES-MORENO, M. C., MUGA, R., TORRENS, M. & FARRÉ, M. 2018. Cannabinoids: from pot to lab. *Int J Med Sci,* 15**,** 1286-1295.

PEACE, M. R., KRAKOWIAK, R. I., WOLF, C. E., POKLIS, A. & POKLIS, J. L. 2017. Identification of MDMB-FUBINACA in commercially available e-liquid formulations sold for use in electronic cigarettes. *Forensic Sci Int,* 271**,** 92-97.

RANGARI, V. A., O'BRIEN, E. S., POWERS, A. S., SLIVICKI, R. A., BERTELS, Z., APPOURCHAUX, K., AYDIN, D., RAMOS-GONZALEZ, N., MWIRIGI, J., LIN, L., MANGUTOV, E., SOBECKS, B. L., AWAD-AGBARIA, Y., UPHADE, M. B., AGUILAR, J., PEDDADA, T. N., SHIIMURA, Y., HUANG, X. P., FOLARIN-HINES, J., PAYNE, M., KALATHIL, A., VARGA, B. R., KOBILKA, B. K., PRADHAN, A. A., CAMERON, M. D., KUMAR, K. K., DROR, R. O., GEREAU, R. W. T. & MAJUMDAR, S. 2025. A cryptic pocket in CB1 drives peripheral and functional selectivity. *Nature,* 640**,** 265-273.

REDDIT. 2025. *MDMB-FUBINACA* [Online]. User reports available at: https://www.reddit.com/r/noids/comments/f1mi25/anyone_know_whats_the_strongest_noid_or_synthetic/; https://www.reddit.com/r/researchchemicals/comments/3xxziw/anyone_try_fub_mdmb/; https://www.reddit.com/r/noids/comments/18tadbk/which_of_these_5fadb_mdmbchminaca_mdmbfubinaca/. [Accessed August 13 2025].

SCHOEDER, C. T., HESS, C., MADEA, B., MEILER, J. & MÜLLER, C. E. 2018. Pharmacological evaluation of new constituents of "Spice": synthetic cannabinoids based on indole, indazole, benzimidazole and carbazole scaffolds. *Forensic Toxicol,* 36**,** 385-403.

SELWE, K. P., SHAIKH, A. S. A., ULEANYA, K. O. & DESSENT, C. E. H. 2025. Fragmentation and Isomerization Pathways of Natural and Synthetic Cannabinoids Studied via Higher Collisional Energy Dissociation Profiles. *Molecules,* 30**,** 717.

UNITED NATIONS OFFICE ON DRUGS AND CRIME. 2025a. *Early Warning Advisory (EWA) on New Psychoactive Substances: MDMB-FUBINACA* [Online]. Logged into site at

https://www.unodc.org/LSS/Home/NPS and used search term "MDMB-FUBINACA". [Accessed July 29 2025].

UNITED NATIONS OFFICE ON DRUGS AND CRIME. 2025b. *Early Warning Advisory (EWA) Tox-Portal: MDMB-FUBINACA* [Online]. Logged into site at https://www.unodc.org/tox/#/login and used search term "MDMB-FUBINACA". [Accessed August 13 2025].

WELSH EMERGING DRUGS AND IDENTIFICATION OF NOVEL SUBSTANCES PROJECT. 2025. *MDMB-FUBINACA* [Online]. Results available at: https://www.wedinos.org/sample-results#mylocation. [Accessed August 13 2025].