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# 5F-MDMB-PINACA

## EMCDDA–Europol Joint Report on a new psychoactive substance: methyl 2-{[1-(5-fluoropentyl)-1*H*-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate (5F-MDMB-PINACA; 5F-ADB)

In accordance with Article 5 of Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances

**About this series**

EMCDDA–Europol Joint Report publications examine the detailed information provided by the EU Member States on individual new psychoactive substances. Information is collected from the Reitox network, the Europol National Units and the national competent authorities of the European Medicines Agency.

Each Joint Report serves as the basis upon which the decision to conduct a risk assessment of the new psychoactive substance is taken. It is part of the three-step procedure involving information exchange, risk assessment and decision-making in the framework of Council Decision 2005/387/JHA.

EUROPOL

EMCDDA–Europol
joint publication

## Contents



## Acknowledgements


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- the Early Warning System (EWS) correspondents of the Reitox national focal points (NFPs) and experts from their national EWS networks;
- the Europol National Units (ENUs) and Europol Project Synergy;
- the national competent authorities responsible for human and veterinary medicinal products in the Member States, Norway and Iceland;
- the European Medicines Agency (EMA) and the European Commission;
- the World Health Organization.

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## 1. Introduction

Article 5.1 of Council Decision 2005/387/JHA [1] (hereinafter the 'Council Decision') stipulates that 'Where Europol and the EMCDDA, or the Council, acting by a majority of its members, consider that the information provided by the Member State on a new psychoactive substance merits the collection of further information, this information shall be collated and presented by Europol and the EMCDDA in the form of a Joint Report.' The Joint Report shall be submitted to the Council of the European Union, the European Medicines Agency (EMA), and the European Commission.

In March 2017, the EMCDDA and Europol examined the available information on the new psychoactive substance methyl 2-{[1-(5-fluoropentyl)-1*H*-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate, commonly known as 5F-MDMB-PINACA, through a joint assessment based upon the following criteria:

1. the amount of the material seized;
2. evidence of organised crime involvement;
3. evidence of international trafficking;
4. analogy with better-studied compounds;
5. evidence of the potential for further (rapid) spread; and,
6. evidence of cases of serious intoxication or fatalities.

The EMCDDA and Europol agreed that the information collected on 5F-MDMB-PINACA satisfied criteria 1, 4, 5 and 6. The two agencies therefore concluded that sufficient information had been accumulated to merit the production of a Joint Report on 5F-MDMB-PINACA as stipulated by Article 5.1 of the Council Decision.

## 2. Information collection process

In compliance with the provisions of the Council Decision, on 25 April 2017 the EMCDDA and Europol launched a procedure for the collection of information on 5F-MDMB-PINACA, in order to prepare the Joint Report. The information was collected mainly through the Reitox national focal points in the Member States, Turkey and Norway as well as the Europol National Units. In addition, the EMA collected information through the national competent authorities responsible for human and veterinary medicinal products in the Member States as well as in Norway, Iceland and Liechtenstein. The EMA also provided information as relevant to the centralised procedure for authorising medicinal products. The information collection process was largely concluded by 6 June 2017.

[1] OJ L 127, 20.5.2005, p. 32.

### Information collected by Europol

Europol asked the Europol National Units to provide information on:

- the level of production of 5F-MDMB-PINACA in their country;
- the level of distribution of 5F-MDMB-PINACA in their country;
- the level of trafficking of 5F-MDMB-PINACA in their country, both for internal, transit or export purposes;
- the number of seizures of 5F-MDMB-PINACA in their country, the total amount of the seizures, country of origin, details on the physical forms (including photos);
- the role of organised crime or criminal groups, in the production, distribution and trafficking of 5F-MDMB-PINACA in their country;
- any known aspect of violence and/or money laundering relating to the production and trafficking of 5F-MDMB-PINACA.

Europol received responses from 15 Member States [2].

### Information collected by the EMA

According to Article 5.3 of the Council Decision, the EMA requested that the national competent authorities responsible for human and veterinary medicinal products in the Member States, Norway, Iceland and Liechtenstein, provide information on whether:

- the new psychoactive substance 5F-MDMB-PINACA has obtained a marketing authorisation;
- the new psychoactive substance 5F-MDMB-PINACA is the subject of an application for a marketing authorisation;
- a marketing authorisation that had been granted in respect of the new psychoactive substance 5F-MDMB-PINACA has been suspended.

Twenty-three countries provided a response to the EMA's request regarding human and/or veterinary medicinal products [3]. The EMA also provided information as relevant to the centralised procedure for authorising human and veterinary medicinal products.

[2] In alphabetical order: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Finland, Germany, Greece, Latvia, Lithuania, Luxembourg, Romania, Slovakiaand Slovenia.

[3] Austria, Belgium, Denmark, Estonia, Finland, Germany, Greece, Ireland, Latvia, Norway, Poland, Spain, Sweden and the United Kingdom provided a response in relation to human and veterinary medicinal products. Croatia, Czech Republic, Hungary, Italy and the Netherlands provided a response in relation to human medicinal products. France, Portugal, Slovakia and Slovenia provided a response in relation to veterinary medicinal products.

Furthermore, in anticipation of Article 7.3 of the Council Decision in relation to the manufacturing of medicinal products in the European Union, the EMA also requested information on whether the new psychoactive substance 5F-MDMB-PINACA is used to manufacture a medicinal product:

- which has been granted a marketing authorisation;
- for which an application has been made for a marketing authorisation;
- for which a marketing authorisation has been suspended by a competent authority.

Twenty-three countries ([4]) provided a response to the EMA's request in this regard. The EMA also provided information as relevant to the centralised procedure for authorising human and veterinary medicinal products.

### Information collected by the EMCDDA

The EMCDDA collected information through:

- a structured questionnaire to the Reitox national focal points. The EMCDDA received replies from 27 Member States ([5]), as well as Turkey and Norway;
- reports previously provided to the European Union Early Warning System, including EMCDDA–Europol Reporting Forms and Progress Reports and Final Reports;
- routine monitoring of open source information;
- a specific information request to the World Health Organization on whether or not 5F-MDMB-PINACA is under assessment by the United Nations system;
- a search of open source information conducted specifically for the production of the Joint Report which included: scientific and medical literature, official reports, grey literature, internet drug discussion forums and related websites (hereafter, 'user websites') and online vendors selling 5F-MDMB-PINACA.

Thus, the information included in sections 3.2.1 and 3.3 of the Joint Report was provided by Europol, while the EMCDDA provided information included in sections 3.1, 3.2.2, 3.4, 3.5, 3.6, 3.7, 3.8.1, 3.8.2 and 3.8.3 (in part). The information included in sections 3.8.3 (in part) and 4 was provided by the EMA. Images of the seizures and collected samples reported to the EMCDDA are provided in Annex 1.

([4]) Austria, Belgium, Denmark, Estonia, Finland, Germany, Greece, Ireland, Latvia, Norway, Poland, Spain, Sweden and the United Kingdom provided a response in relation to human and veterinary medicinal products. Croatia, Czech Republic, Hungary, Italy and the Netherlands provided a response in relation to human medicinal products. France, Portugal, Slovakia and Slovenia provided a response in relation to veterinary medicinal products.
([5]) A reply was not received from Slovakia.

## 3. Information required by Article 5.2 of the Council Decision

The order and titles of subsections 3.1 to 3.8 and section 4, below, are as they appear in Article 5.2(a) to (h) and Article 5.3(a) to (c) of the Council Decision; sections are cross-referenced with those set down in the Council Decision.

### 3.1 Chemical and physical description, including the names under which the new psychoactive substance is known (Article 5.2(a) of the Council Decision)

#### Chemical description and names

Methyl 2-{[1-(5-fluoropentyl)-1*H*-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate is commonly referred to as 5F-MDMB-PINACA and/or 5-ADB ([6]).

5F-MDMB-PINACA is a synthetic cannabinoid receptor agonist. It appears not to have been described in the scientific or patent literature prior to the first detection on the drug market in Europe in 2014.

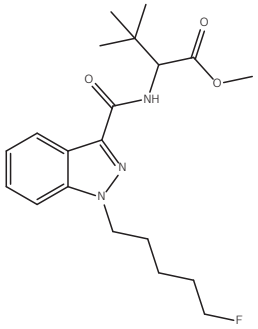
5F-MDMB-PINACA shares some structural features with MDMB-CHMICA ([7]) ([8]), which was risk-assessed in 2016 (EMCDDA, 2016). MDMB-CHMICA will be controlled under Schedule II of the United Nations Convention on Psychotropic Substances of 1971 ([9]).

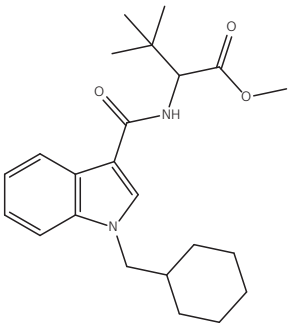
The molecular structure, molecular formula and molecular mass of 5F-MDMB-PINACA are provided in in Figure 1.

([6]) The common name for the substance is derived after its structural features. Different naming systems exist and are used for applying short/code names to synthetic cannabinoids.
([7]) Methyl 2-[[1-(cyclohexylmethyl)-1*H*-indole-3-carbonyl]amino]-3,3-dimethylbutanoate.
([8]) Both substances contain a methyl dimethyl butanoate linked group (MDMB) and a carboxamide linker (CA), however they differ due to the indazole core (INA) and 5-fluoropentyl (5F-P) moiety present in 5F-MDMB-PINACA, whereas MDMB-CHMICA has an indole core (I) with a cyclohexylmethyl moiety (CHM) present.
([9]) Two synthetic cannabinoid receptor agonists have been recently controlled under the Schedule II of the United Nations Convention on Psychotropic Substances of 1971: JWH-018 (naphthalen-1-yl(1-pentyl-1*H*-indol-3-yl) methanone) and AM-2201 (1-(5-fluoropentyl)-1*H*-indol-3-yl]-(naphthalen-1-yl) methanone). In addition, MDMB-CHMICA, 5F-APINACA (5F-AKB48) and XLR-11 will be also included in the same schedule.

FIGURE 1

**Molecular structure, molecular formula and molecular mass of 5F-MDMB-PINACA. Information on MDMB-CHMICA is provided for comparison.**




| | 5F-MDMB-PINACA | MDMB-CHMICA |
|---|---|---|
| Molecular formula | $C_{20}H_{28}FN_3O_3$ | $C_{23}H_{32}N_2O_3$ |
| Molecular mass | 377.46 | 384.52 |

5F-MDMB-PINACA contains a stereocentre thus allowing for the existence of a pair of enantiomers ([10]), (*R*)- and (*S*)-5F-MDMB-PINACA. Based on the patent literature of similar compounds (Buchler et al., 2009) and the most likely precursors to be used, an (*S*)-configuration of the stereocentre could be expected. The synthesis of (*S*)-5F-MDMB-PINACA has been described by Banister et al. (Banister et al., 2016).

There is no representative information on the enantiomeric composition of the samples of 5F-MDMB-PINACA detected within the European Union, which in part may reflect the fact that stereochemical analysis is not routinely undertaken in forensic laboratories. Differentiation of enantiomers is possible using the following techniques: chiral chromatography, vibrational circular dichroism (VCD) spectroscopy and/or electronic circular dichroism (ECD) spectroscopy.

*Commonly used names:*
5F-MDMB-PINACA; 5F-ADB

*Systematic (IUPAC) name:*
methyl 2-{[1-(5-fluoropentyl)-1*H*-indazole-3-carbonyl]amino}-3,3-dimethylbutanoate

*Other chemical names ([11]):*
methyl 2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate;
methyl-[2-(1-(5-fluoropentyl)-1H-indazole-3-carboxamido)-3,3-dimethylbutanoate];
N-[1-(aminocarbonyl)-2,2-dimethylpropyl]-1-(5-fluoropentyl)-1H-indazole-3-carboxamide;
valine, N-[[1-(5-fluoropentyl)-1H-indazol-3-yl]carbonyl]-3-methyl-, methyl ester;
1-(5-fluoropentyl)-3-(2-(methyl 3,3-dimethylbutanoate) carbamoyl)indazole;
metyl-2-(1-(5-fluoropentyl)-1H-indazol-3-karboxamido)-3,3-dimetylbutanoat (Sweden)

*Other names and code names:*
5F-methyl-AMB; 5-fluoro-MAMB; 5-fluoro ADB; 5-fluoro MDMB-PINACA; MDMB(N)-2201; 5FADB

*Chemical Abstracts Service (CAS) registry numbers* ([12]):

| | |
|---|---|
| 1715016-75-3 | 5F-MDMB-PINACA racemate |
| 1838134-16-9 | (*R*)-5F-MDMB-PINACA |
| 1971007-89-2 | (*S*)-5F-MDMB-PINACA |

*IUPAC International Chemical Identifier Key (InCHI Key)* ([13]*):*

| | |
|---|---|
| PWEKNGSNNAKWBL-UHFFFAOYSA-N | 5F-MDMB-PINACA racemate |
| PWEKNGSNNAKWBL-KRWDZBQOSA-N | (*R*)-5F-MDMB-PINACA |
| PWEKNGSNNAKWBL-QGZVFWFLSA-N | (*S*)-5F-MDMB-PINACA |

The REACH registered substances database hosted by the European Chemicals Agency (ECHA) was searched using the CAS registry numbers listed above. The searches returned no hits.

([10]) Optical isomers (or enantiomers) have the same physico-chemical characteristics, differing only in their interaction with plane polarized light.
([11]) Names listed do not take into account the enantiomeric composition.

([12]) The Chemical Abstract Service Registry Number (CAS RN) is a unique numeric identifier assigned by the Chemical Abstract Service Division of the American Chemical Society to a specific, single chemical substance.
([13]) InChI Key is a unique, non-proprietary stuctural identifier of chemical substances useful in electronic sources.

### Physical description

In its pure form, 5F-MDMB-PINACA is a white solid (Banister et al., 2016). It is soluble in dichloromethane (DCM), methanol (MeOH) and partially soluble in water (Slovenian National Forensic Laboratory, 2016). It is soluble up to approximately 25 mg/mL in ethanol, dimethyl sulfoxide (DMSO) and dimethyl formamide (DMF) and sparingly soluble in aqueous buffers (Cayman Chemical Company).

The measured melting point for 5F-MDMB-PINACA is 64-66°C (Banister et al., 2016). The boiling point has been estimated to be below 350°C according to its retention time in GC-MS analysis (Moosmann et al., 2017).

5F-MDMB-PINACA has been typically seized as a herbal material and in powder form. It has also been detected in liquids and blotters. A more detailed description of seizures and collected samples can be found in section 3.2.1 and section 3.2.2.

#### Chemical stability and typical reactions

For long term storage it is recommended that 5F-MDMB-PINACA, supplied as a solution in acetonitrile, is stored at -20°C (Cayman Chemical Company).

Storage under non-ideal conditions (e.g. high humidity or elevated temperatures) or in solution can lead to hydrolysis of the carboxylic ester function. Ester hydrolysis can also be expected to occur during smoking (Moosmann et al., 2017).

### Detection and analysis

Reference materials are claimed to be available for (*R*)-5F-MDMB-PINACA ([14]) and for (*S*)-5F-MDMB-PINACA ([15]).

Methods documented in the literature for the detection of 5F-MDMB-PINACA include:

- gas chromatography–mass spectrometry (GC-MS), high performance liquid chromatography time-of-flight (HPLC-TOF), Fourier transform infrared spectroscopy attenuated total reflectance (FTIR-ATR), gas chromatography – mass spectrometry– infrared (GC-MS-IR) condensed phase and ion chromatography (IC) applied to the analysis of powder (Slovenian National Forensic Laboratory 2017)
- GC-MS, high-resolution mass spectrometry (GC–HRMS), ultra-high-performance liquid chromatography–high-resolution tandem mass spectrometry (UHPLC–HRMS) and $^{1}H$ and $^{13}C$ nuclear magnetic resonance spectroscopy (NMR) applied to powder and plants (Shevyrin et al., 2015)
- liquid chromatography–tandem mass spectrometry (LC–MS–MS) and GC-MS applied to biological samples (Hasegawa et al., 2015).

Quantification of 5F-MDMB-PINACA in products can be carried out according to the general procedure described by the UNODC (UNODC, 2013).

## 3.2 Information on the frequency, circumstances and/or quantities in which a new psychoactive substance is encountered, and information on the means and methods of manufacture of the new psychoactive substance (Article 5.2(b) of the Council Decision)

The data reported to Europol discussed in section 3.2.1 may overlap with the data reported to the EMCDDA discussed in section 3.2.2.

### 3.2.1 Information provided to Europol

Europol received replies from 15 Member States (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Finland, Germany, Greece, Latvia, Lithuania, Luxembourg, Romania, Slovakia and Slovenia).

Five countries reported that they have no available information on 5F-MDMB-PINACA (Croatia, Cyprus, Greece, Latvia and Luxembourg).

The remaining 10 countries provided information on 5F-MDMB-PINACA (Austria, Belgium, Bulgaria, Czech Republic, Finland, Germany, Lithuania, Romania, Slovakia and Slovenia).

#### The level of production

No information was received in relation to the production of 5F-MDMB-PINACA.

#### The level of distribution

- At least 240 seizures were reported by nine Member States: Austria (3), Belgium (6), Bulgaria (1), Czech Republic (2), Finland (exact number unspecified), Germany (220), Lithuania (4), Romania (at least 2, exact number unspecified) and Slovakia (1). Slovenia reported a collected sample (section 3.2.2);
- Austria: 3 seizures made in 2016, the country of origin was China;
- Belgium: 6 customs seizures made in 2017 at Bierset airport, amounting to 2.55 kg;

([14]) Cayman Chemical Company. '5-fluoro ADB', https://www.caymanchem.com/product/16603

([15]) Chiron. However, the CAS number (1715016-75-3) listed for the (*S*) enantiomer corresponds to the racemate. http://shop.chiron.no/main.aspx?page=article&artno=C11345.20-10MG&gid=13277&gidlevel=3&pid=

- Bulgaria: 1 seizure of powder amounting to 10 g, which was delivered from Spain to Bulgaria in a package labelled '5F ADB 10g Legal Research Chemical Reagent Use Only';
- Czech Republic: 2 seizures made in 2016 and 2017, via express courier to Israel, amounting to 498 and 445 g, respectively;
- Finland: unspecified number of seizures made in 2016;
- Germany: 189 small seizures made in 2016, most of which were in the form of herbal material ('legal high' products); and 31 seizures in 2017, most of which were in the form of herbal material. One of the seizures in 2017 was made by customs and amounted to over 1 kg of powder;
- Lithuania: 4 seizures made in 2017, which amounted to almost 2 kg;
- Romania: reported and unspecified number of seizures in 2015 and 2016, amounting to over 2 and 10 kg, respectively;
- Slovakia: 1 seizure of lump material made in 2017, amounting to 500 g.

**The level of trafficking**

Information related to trafficking routes is limited to the seizures reported above.

### 3.2.2 Information provided to the EMCDDA

The EMCDDA received responses from 27 Member States ([5]), as well as from Turkey and Norway. Of these, 26 Member States, Turkey and Norway ([16]) reported detections of 5F-MDMB-PINACA ([17]).

It is important to note that detections of 5F-MDMB-PINACA may be under-reported since the substance is not routinely screened for. Three Member States (Austria, Slovenia and Sweden) and Norway reported that 5F-MDMB-PINACA is part of routine screening in some (but not all) of their laboratories.

**Seizures**

In total, 1 986 seizures of 5F-MDMB-PINACA were reported to the EMCDDA by 21 Member States, Norway and Turkey: Austria (1 seizure), Belgium (9), Bulgaria (11), Czech Republic (1), Denmark (1), Estonia (1), Finland (8), France (16), Germany (1), Greece (3), Hungary (252), Ireland (36), Lithuania (27), Latvia (1), Malta (3), the Netherlands (1), Poland (58), Romania (3), Spain (8), Sweden (71), the United Kingdom (1252), Norway (13) and Turkey (209) ([18]). The majority of the seizures comprise police and customs cases, with additional seizures taking place in custodial settings.

Seizures included herbal materials, powders, liquids, blotters and unspecified physical forms. A summary is provided below.

*Herbal material*

- 1 485 seizures of 5F-MDMB-PINACA in herbal material were reported by 16 countries: Bulgaria, Germany, Greece, Finland, France, Hungary, Ireland, Lithuania, Latvia, Malta, Norway, Poland, Romania, Spain, Sweden and the United Kingdom, amounting to 26 kg seized ([19]). In addition, Turkey reported 209 seizures of herbal material amounting to almost 74 kg ([20]).
- The largest single seizures of 5F-MDMB-PINACA in herbal material were reported by: Romania (2.9 kg which also contained MDMB-CHMICA) and the United Kingdom (2.4 kg).
- In 2 seizures reported by Police Scotland (UK), a total of 7 669 sealed foil packages (~10 kg), of commercially labelled herbal materials were seized. The following products were seized: 'Exodus Damnation 1G' (5 198 packages), 'Exodus Damnation 3G' (1 106 packages), 'Exodus Nightshade 1G' (1 197 packages), 'Exodus Nightshade 3G' (168 packages), 'Vertex Space Cadet Edition 1G' (20 packages). A small number of samples of each product were analysed and were found to contain 5F-MDMB-PINACA, mixed with 5F-AMB-PICA (not confirmed analytically).
- In the herbal materials seized, 5F-MDMB-PINACA was commonly found mixed with other synthetic cannabinoids. In two cases reported by the United Kingdom, the synthetic opioid U-47,700 was also detected in herbal materials mixed with 5F-MDMB-PINACA.
- The United Kingdom reported 129 seizures of 5F-MDMB-PINACA that took place in a prison or other custodial setting, amounting to a total of 3 kg of mostly herbal material and often in combination with other synthetic cannabinoids.

*Powder*

- 77 seizures of powder were reported by 12 countries (Belgium, Bulgaria, Czech Republic, Finland, France, Hungary, Ireland, Lithuania, the Netherlands, Poland, Sweden and the United Kingdom) amounting to a total of more than 13.4 kg.
- The largest single seizures of 5F-MDMB-PINACA in powder form were reported by: Bulgaria (2 kg of white powder, seized in April 2016 by customs at Sofia Airport), France

([16]) Two Member States (Cyprus and Slovakia) reported no detections of 5F-MDMB-PINACA.
([17]) 'Detections' is an all-encompassing term and may include seizures and/or collected and/or biological samples that are analytically confirmed. Seizure means a substance available (seized) through law enforcement activities (police, customs, border guards, etc.). Collected samples are those that are actively collected by drug monitoring systems (such as test purchases) for monitoring and research purposes. Biological samples are those from human body fluids (urine, blood, etc.) and/or specimens (tissues, hair, etc.).

([18]) Minimum estimate provided by the Turkish national focal point.
([19]) No amounts were reported for 686 detections reported by LGC in the UK for the year 2016, so the total amount is likely to be considerably higher.
([20]) This is a minimum estimate provided by the Turkish National Focal Point.

(2 seizures over 2 kg, one of which was 2.3 kg of brown powder seized by customs in March 2017 at Roissy airport) and the Netherlands (2 kg seized by customs). Additionally, 8 customs seizures of powders weighing more than 1 kg each were reported by Belgium (2 seizures) and France (2). The seizures were all carried out at international airports.

*Liquid*

- Nine seizures of 5F-MDMB-PINACA in liquid form were reported by six countries: Denmark, Estonia, Finland, Norway, Sweden and the United Kingdom, amounting to a total 309.2 g and 94 ml seized.
- In a 274 g seizure reported by the UK, the liquid (clear and yellow) also contained U-47,700.
- Two bottles (of 5 ml each) of C-liquid for vaping were seized by customs in Denmark. The bottles originated in Spain, with Denmark as the final destination.
- Two bottles (7 ml each) of a pink liquid named "SKITTLES" were seized by Norwegian customs.

*Other physical forms*

- Small amounts of 5F-MDMB-PINACA in blotter form were reported by Poland (2 seizures) and Lithuania (1).
- Additionally, in 287 cases, amounting to more than 3.5 kg, the physical form was unspecified.

Quantitative information on purity of 5F-MDMB-PINACA in seized samples was reported by Lithuania for two samples of powder: 96 % purity (for a sample of 141.01 g) and 91 % (sample of 0.9835 g).

**Collected samples**

Nine collected samples were reported by five Member States: Germany (4 cases), Italy (1), Luxembourg (1), Slovenia (1) and the United Kingdom (2). The detections included small amounts of herbal material, powder and one joint. Where reported, the samples were either collected in relation to cases of acute intoxications or as test purchases from online vendors.

The sample reported by Slovenia consisted of 5 g of white powder purchased as '5F-NPB-22' and shipped from Germany.

The United Kingdom reported a test purchase of a product named 'K2 Black edition', purchased from a domestic website.

**Biological samples**

Serious adverse events with confirmed exposure to 5F-MDMB-PINACA from biological samples are discussed in section 3.4.2.

In addition to these, 84 detections where 5F-MDMB-PINACA was analytically confirmed in biological samples were reported by two Member States: Hungary (83) and Sweden (1) ([21]). Detections include:

- 15 cases of persons suspected of driving under the influence of drugs (including three traffic accidents), all reported by Hungary;
- 69 cases reported as aggregated data associated with forensic case work (details not specified).

## 3.3 Information on the involvement of organised crime in the manufacture or trafficking of the new psychoactive substance (Article 5.2(c) of the Council Decision)

No information concerning the involvement of organised crime in the manufacture and/or trafficking of the 5F-MDMB-PINACA was provided.

**Money laundering aspects**

No information was received on money laundering in connection with the production and/or trafficking of 5F-MDMB-PINACA.

**Violence in connection with production, wholesale and distribution**

No information was received on incidents of violence in connection with the production, wholesale and/or trafficking of 5F-MDMB-PINACA.

## 3.4 A first indication of the risks associated with the new psychoactive substance, including the health and social risks, and of the characteristics of users — Article 5.2(d) of the Council Decision

### 3.4.1 Health risks

**Pharmacology and toxicology**

Limited data suggests that 5F-MDMB-PINACA is a $CB_1$ receptor agonist (Banister et al., 2016; Moosmann et al., 2017; US DEA, 2016 ([22])) that shares some similarities with the major psychoactive constituent of cannabis (–)-*trans*-$\Delta^9$-tetrahydrocannabinol (THC) and synthetic cannabinoids such as JWH-018 and MDMB-CHMICA (EMCDDA, 2017; Järbe and Raghav, 2017; Pertwee, 2014; Reggio, 2009).

([21]) In addition, Turkey reported 113 samples (blood, hair and urine) which may contain duplicates and therefore have not been included in the total count.
([22]) Where reported the (*S*) enantiomer was studied.

The acute effects of THC (and consequently cannabis) include: relaxation, euphoria, lethargy, depersonalisation, distorted perception of time, impaired motor performance, hallucinations, paranoia, confusion, fear, anxiety, dry mouth, reddening of the conjunctivae of the eyes, tachycardia, nausea and vomiting. THC also has an abuse liability and dependence potential (Pertwee, 2014; Wiley et al., 2016). Similar effects to cannabis have been reported for synthetic cannabinoids such as 5F-MDMB-PINACA. In some cases, the effects are reported to be more pronounced/severe (EMCDDA, 2017b).

Compared to cannabis, severe and fatal poisoning appears to be more common with synthetic cannabinoids (EMCDDA, 2017b; Tait et al., 2016). Poisoning may include rapid loss of consciousness/coma, cardiovascular effects (such as hypertension, tachycardia, bradycardia, chest pain, myocardial infarction and stroke), seizures and convulsions, vomiting/hyperemesis, delirium, agitation, psychosis and aggressive and violent behaviour. Sudden death has also been reported. The mechanisms of this toxicity are poorly understood (Tai and Fantegrossi, 2016), but factors that are likely to play an important role are the potency of the substances and the doses that users are exposed to. In addition, some of the effects of poisoning — such as loss of consciousness or behavioural effects — may place users at additional risks such as choking on vomitus, drowning or self-harm.

There is no antidote to poisoning caused by synthetic cannabinoids.

In general, the use of herbal smoking mixtures containing synthetic cannabinoids appears to pose a high risk of poisoning. This is because manufacturers guess the amount of cannabinoid(s) to add to the herbal material and the manufacturing process makes it difficult to dilute them sufficiently and distribute them consistently throughout the material. This can result in mixtures that contain a large amount of highly potent cannabinoid, as well as 'hot pockets' where the cannabinoid is highly concentrated within parts of the herbal material (e.g. Schäper et al., 2016). Together, this makes it difficult for users to control the dose that they are exposed to. As these mixtures are typically smoked as cigarettes ('joints'), users can inadvertently administer a toxic dose; in some cases, a small number of puffs from a cigarette have been sufficient to cause severe poisoning. Reflecting these risks, smoking mixtures have caused a large number of outbreaks of mass poisonings in recent years (Adams et al., 2017; Kasper et al., 2015; Schwartz et al., 2015; Shevyrin et al., 2015; Trecki et al., 2015; Tyndall et al., 2015).

While there is limited data for 5F-MDMB-PINACA, the chronic health risks might share similarities to cannabis and other synthetic cannabinoids. This may include dependence.

### 3.4.2 Serious adverse events

#### Acute intoxications

A total of 35 acute intoxication with confirmed exposure to 5F-MDMB-PINACA were reported by Hungary (1 case) and the United Kingdom (34 cases) ([23]). The cases occurred during 2016. No further details are available on the case from Hungary.

In six of the cases from the United Kingdom, no other substances were detected. In the remaining cases, other synthetic cannabinoids (detected in 20 cases) and opioids (with methadone detected in 19 cases) were typically detected. Overall, many of the cases included clinical features of poisoning similar to those reported for synthetic cannabinoids.

#### Deaths

A total of 24 deaths with confirmed exposure to 5F-MDMB-PINACA were reported by Germany (16 cases) and United Kingdom (8). The cases occurred between 2015 and 2017.

Of the deaths, 22 were male (92 %), one was female (4 %); the data was missing for one case (4 %). The males were aged between 22 and 49 years (mean 33.1, median 31.5); the female was aged 48.

In five cases, no other substances were detected. In the remaining cases, other substances were detected; for many this included central nervous system depressants (such as alcohol, synthetic cannabinoids and opioids). Where known, many of the cases were found dead; in at least some cases the individuals were in a home environment or prison. In at least 14 cases, 5F-MDMB-PINACA was the cause of death or contributed to the death.

### 3.4.3 Characteristics of users

Similar to other synthetic cannabinoids, 5F-MDMB-PINACA is sold and used as a 'legal' substitute for cannabis (EMCDDA, 2009; EMCDDA, 2017). The most common way of using it is by smoking a cigarette of herbal mixture that has been laced with the substance. Because these products rarely state the ingredients, most users will be unaware that they are using 5F-MDMB-PINACA.

People who use 5F-MDMB-PINACA may include recreational users, high-risk drug users and groups who experiment with the substance (such as psychonauts). This may also include

([23]) In addition, Germany reported 5 acute intoxications with possible exposure to ADB-CHMINACA and Italy reported 1 acute intoxication with possible exposure to ADB-CHMINACA. These cases are not discussed further in this report.

individuals who are subject to drug testing (such as people in drug treatment, prisoners and drivers) because some drug tests/screens will be unable to detect 5F-MDMB-PINACA. In the past few years, synthetic cannabinoids have become increasingly used by vulnerable groups (such as the homeless and prisoners).

### 3.4.4 Social risks

While there is limited data for 5F-MDMB-PINACA, the social risks might share some similarities with cannabis and other synthetic cannabinoids.

Of particular note is that synthetic cannabinoids are increasingly used by vulnerable groups, such as the homeless and prisoners. Reports suggest that this has caused new health and social problems as well as exacerbated existing ones for these groups. For example, in prisons, alongside the adverse health effects, the market in synthetic cannabinoids has been linked to an increase in aggression, violence, bullying and debt. In some cases this has caused a serious threat to the overall safety and security of the prison environment (Blackman et al., 2017; HMIP, 2015; Ralphs et al., 2017; User Voice, 2016).

## 3.5 Information on whether or not the new substance is currently under assessment, or has been under assessment, by the UN system (Article 5.2(e) of the Council Decision)

The World Health Organization is the specialised United Nations agency designated for the evaluation of the medical, scientific and public health aspects of psychoactive substances under the Single Convention on Narcotic Drugs, 1961 and the Convention on Psychotropic Substances, 1971.

On 1 May 2017, the World Health Organization (WHO) informed the EMCDDA that 5F-MDMB-PINACA is currently not under assessment and has not been under assessment by the UN system.

On 12 May 2017, the WHO informed the EMCDDA that '5F-ADB' will be assessed at the 39th meeting of the WHO Expert Committee on Drug Dependence (ECDD) that will be held on 16–20 November 2017. At the time of writing this report neither a critical review nor a written recommendation had been published.

## 3.6 The date of notification on the Reporting Form of the new psychoactive substance to the EMCDDA or to Europol (Article 5.2(f) of the Council Decision)

The first official EMCDDA–Europol notification of 5F-MDMB-PINACA dates from 8 January 2015 from the Hungarian national focal point. The Reporting Form details a seizure of 0.79 g of white powder that was seized in September 2014 by the National Tax and Customs Administration Airport Directorate Nr.1, in Budapest. The substance was analytically confirmed by GC-MS and Fourier transform infrared spectroscopy (FT-IR).

5F-MDMB-PINACA was added to the list of new psychoactive substances monitored by the EMCDDA and Europol through the European Union Early Warning System. A profile of the substance was created on the European Database on New Drugs (EDND). Since then, analytical details and other information, including a public health alert, have been exchanged between the EMCDDA, Europol, and the Member States, Turkey and Norway, on an ad hoc basis; the European Commission and the EMA have been kept duly informed.

## 3.7 Information on whether or not the new psychoactive substance is already subject to control measures at national level in a Member State (Article 5.2(g) of the Council Decision)

Twelve Member States (Bulgaria, Croatia, Cyprus, Czech Republic, Estonia, Finland, France, Germany, Latvia, Lithuania, Luxembourg and Sweden) reported that 5F-MDMB-PINACA is controlled under drug control legislation.

Three Member States (Austria, Hungary and Poland) and Turkey reported that 5F-MDMB-PINACA is controlled under specific new psychoactive substances control legislation.

Twelve Member States (Belgium, Denmark, Greece, Ireland, Italy, Malta, the Netherlands, Portugal, Romania, Slovenia, Spain and the United Kingdom) reported that 5F-MDMB-PINACA is not subject to control measures at the national level.

Norway reported that 5F-MDMB-PINACA is controlled under medicinal products legislation.

Slovakia did not provide information on the control status of 5F-MDMB-PINACA.

## 3.8 Further information (Article 5.2(h) of the Council Decision)

### 3.8.1 The chemical precursors that are known to have been used for the manufacture of the substance

No information was reported by the Member States, Turkey or Norway, about the chemical precursors or manufacturing methods used to make the 5F-MDMB-PINACA which has been detected within Europe.

The synthesis of (*S*)-5F-MDMB-PINACA enantiomer was described by Banister et al. starting from the commercially available methyl 1*H*-indazole-3-carboxylate which was reacted with methyl L-*tert*-leucinate (Banister et al., 2016). Other 1*H*-indazole-3-carboxylic acid esters might be suitable as alternative starting materials. The (*R*) enantiomer might be synthesised under identical conditions using methyl D-*tert*-leucinate instead of methyl L-*tert*-leucinate. Using methyl *tert*-leucinate as a racemate would lead to racemic 5F-MDMB-PINACA. The reported synthesis route is comparable to the way Buchler et al. described the synthesis of other structurally related indazole derivatives in a patent application (Buchler et al., 2009).

According to Buchler et al. (Buchler at al., 2009) the starting compound methyl 1*H*-indazole-3-carboxylate, which is commercially available, can be prepared from 1*H*-indole-2,3-dione using the procedure of Johnson et al. (Johnson et al., 2005).

In summary, potential precursors of 5F-MDMB-PINACA are 1*H*-indole-2,3-dione ([24]), 1*H*-indazole-3-carboxylic acid, methyl 1*H*-indazole-3-carboxylate, methyl L-tert-leucinate (for synthesis of the (S)-enantiomer) and 1-bromo-5-fluoropentane (Moosmann et al., 2017).

### 3.8.2 The mode and scope of the established or expected use of the new substance

No studies were identified that have examined the mode and scope of established or expected use of 5F-MDMB-PINACA. Given the limited information currently available, the relevant information has been included in the previous sections.

### 3.8.3 Other use of the new psychoactive substance and the extent of such use, the risks associated with this use of the new psychoactive substance, including the health and social risks

No information was provided by the Member States, Turkey or Norway that indicated that 5F-MDMB-PINACA had any other use apart from in analytical reference materials and scientific research.

From the available information, it does not appear that 5F-MDMB-PINACA is used in the manufacture of a medicinal product in the European Union. However, the data collection is incomplete and some countries indicated that this information is not known. It is understood that the collection of such information is a challenge in the absence of a database on the synthetic route of all medicinal products.

Eleven countries (Austria, Belgium, Croatia, Denmark, Finland, Greece, Italy, the Netherlands, Poland, Spain and the United Kingdom) reported that 5F-MDMB-PINACA is not used to manufacture a medicinal product for human use. Eight countries (Czech Republic, Estonia, Germany, Hungary, Ireland, Latvia, Norway and Sweden) reported that it was unknown if 5F-MDMB-PINACA is used to manufacture a medicinal product for human use.

In addition, the EMA reported that it is not known if 5F-MDMB-PINACA is used in the manufacture of medicinal products for human use and which are centrally authorised within the European Union.

Eleven countries (Austria, Belgium, Denmark, Finland, France, Greece, Latvia, Poland, Slovakia, Spain and the United Kingdom) provided information that 5F-MDMB-PINACA is not used to manufacture a medicinal product for veterinary use. Seven countries (Estonia, Germany, Ireland, Norway, Portugal, Slovenia and Sweden) reported that it was unknown if 5F-MDMB-PINACA is used to manufacture a medicinal product for veterinary use.

In addition, the EMA reported that it is not known if 5F-MDMB-PINACA is used in the manufacture of medicinal products for veterinary use and which are centrally authorised within the European Union.

([24]) A pre-precursor.

## 4. Information from the EMA (Article 5.3 of the Council Decision)

Nineteen countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Ireland, Italy, Latvia, the Netherlands, Norway, Poland, Spain, Sweden and the United Kingdom) reported that:

- 5F-MDMB-PINACA has not been granted a marketing authorisation as a medicinal product for human use;
- 5F-MDMB-PINACA is not the subject of an application for a marketing authorisation as a medicinal product for human use;
- there had been no cases of suspended marketing authorisation in respect to 5F-MDMB-PINACA as a human medicine.

Eighteen countries (Austria, Belgium, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Latvia, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom) reported that:

- 5F-MDMB-PINACA has not been granted a marketing authorisation as a medicinal product for veterinary use;
- 5F-MDMB-PINACA is not the subject of an application for a marketing authorisation as a medicinal product for veterinary use;
- there had been no cases of suspended marketing authorisation in respect to 5F-MDMB-PINACA as a veterinary medicine.

The EMA also reported that 5F-MDMB-PINACA:

- has not been granted a marketing authorisation as a medicinal product for neither human nor veterinary use through the centralised procedure;
- is not the subject of an application for a marketing authorisation for neither human nor veterinary use through the centralised procedure;
- is not the subject of a suspended marketing authorisation for neither human nor veterinary use through the centralised procedure.

## 5. Conclusion

5F-MDMB-PINACA is a synthetic cannabinoid and a $CB_1$ receptor agonist. It shares some pharmacological similarities with $\Delta^9$-tetrahydrocannabinol (THC), which is responsible for the major psychoactive effects of cannabis. In humans, 5F-MDMB-PINACA appears to cause effects that resemble those of cannabis and other synthetic cannabinoids.

5F-MDMB-PINACA has been available in the European Union since at least September 2014 and has been detected in 26 Member States, Turkey and Norway. More than 1 700 seizures have been made within the European Union, which include over 13 kg of powder and 26 kg of herbal material which has been laced with 5F-MDMB-PINACA. This herbal material is typically sold as smoking mixtures; the products are marketed as 'legal' replacements to cannabis. Due to the way that these products are produced, it appears that users are at risk of serious poisoning. There are indications that the 5F-MDMB-PINACA available on the market was synthesised by chemical companies based in China.

Twenty-four deaths with confirmed exposure to 5F-MDMB-PINACA have been reported by two Member States. In at least 14 of the deaths, 5F-MDMB-PINACA was the cause of death or contributed to the death.

5F-MDMB-PINACA is under assessment within the United Nations system. It will be assessed at the 39th meeting of the WHO Expert Committee on Drug Dependence (ECDD) that will be held in November 2017. Currently, neither a critical review nor a written recommendation had been published. 5F-MDMB-PINACA is not subject to control measures in nine Member States.

We conclude that the health and social risks caused by the manufacture, trafficking and use of 5F-MDMB-PINACA and the involvement of organised crime and possible consequences of control measures, could be thoroughly assessed through a risk assessment procedure in accordance with Article 6 of Council Decision 2005/387/JHA.

The EMCDDA and Europol will continue to intensively monitor 5F-MDMB-PINACA in order to ensure that new information is provided to the Member States, the EMA and the Commission via the information exchange of the European Union Early Warning System.

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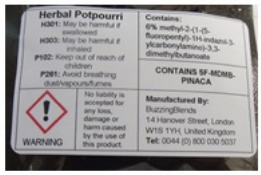
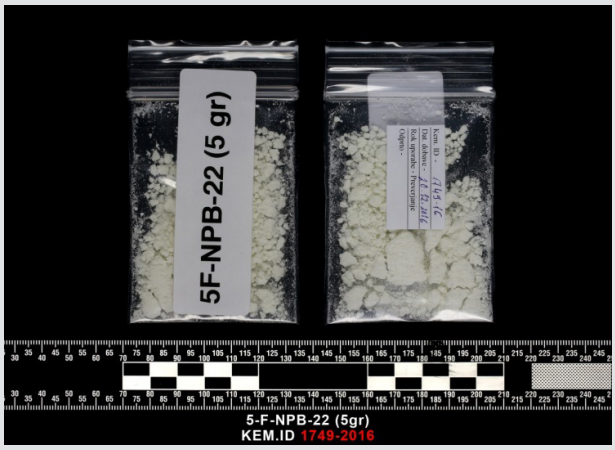
# Annex 1

Images from seizures and collected samples provided to the EMCDDA

| Country | Image | Description |
|---|---|---|
| France |    | **Seizure, 04 February 2016**<br>Green herbal mixture, seized at Saint Denis airport (La Réunion)<br>Seizing authority: Customs |
| Norway |    | **Seizure, 29 February 2016**<br>Herbal mixture in package labelled "Dutchy", seized in Lørenskog<br>Seizing authority: Customs |
| United Kingdom |  | **Collected sample, 10 March 2016**<br>Green herbal mixture<br>Collecting authority: TICTAC Communications |
| Slovenia |  | **Collected sample, 20 December 2016**<br>White powder<br>Collecting authority: project RESPONSE (note: sample was purchased as 5F-NPB-22) |

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The Joint Report represents a legal document, prepared in cooperation with the Council, EMA, and Commission and is published in the original version that has not been edited.

## About the EMCDDA

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) is the central source and confirmed authority on drug-related issues in Europe. For over 20 years, it has been collecting, analysing and disseminating scientifically sound information on drugs and drug addiction and their consequences, providing its audiences with an evidence-based picture of the drug phenomenon at European level.

The EMCDDA's publications are a prime source of information for a wide range of audiences including: policymakers and their advisors; professionals and researchers working in the drugs field; and, more broadly, the media and general public. Based in Lisbon, the EMCDDA is one of the decentralised agencies of the European Union.

## Related publications and websites

**EMCDDA**

- *European Drug Report 2017: Trends and developments*, 2017

**EMCDDA and Europol**

- *EMCDDA–Europol 2016 Annual Report on the implementation of Council Decision 2005/387/JHA*, Implementation reports, 2017

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