



European Monitoring Centre  
for Drugs and Drug Addiction

JOINT REPORTS

ISSN 1977-7868

# MDMB-CHMICA

EMCDDA–Europol Joint Report on a new psychoactive substance: methyl 2-[[1-(cyclohexylmethyl)indole-3-carbonyl]amino]-3,3-dimethylbutanoate (MDMB-CHMICA)

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.

## Contents

3	1. Introduction
3	2. Information collection process
4	3. Information required by Article 5.2 of the Council Decision
4	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)
6	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)
6	3.2.1. Information provided to Europol
8	3.2.2. Information provided to the EMCDDA
9	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)
10	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
10	3.4.1. Serious adverse events reported to the EMCDDA
11	3.4.2. Pharmacology
13	3.4.3. Toxicology
13	3.4.4. Characteristics of users
14	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)
15	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)
15	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)
16	3.8. Further information (Article 5.2(h) of the Council Decision)
16	3.8.1. The chemical precursors that are known to have been used for the manufacture of the substance
16	3.8.2. The mode and scope of the established or expected use of the new substance
16	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
16	4. Information from the EMA (Article 5.3 of the Council Decision)
16	4.1. Marketing authorization
17	4.2. Application for a marketing authorization
17	4.3. Suspended marketing authorization
17	5. Conclusion
18	6. References

## Acknowledgements

The EMCDDA would like to thank the following for their contribution in producing this publication:

- 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;
- Prof. Dr. Volker Auwärter and Dr. Bjoern Moosmann, Institute of Forensic Medicine, Forensic Toxicology, Medical Center – University of Freiburg, Germany;
- István Ujváry, hon. associate professor, Budapest University of Technology and Economics; hon. associate professor, University of Szeged; iKem BT, Budapest, Hungary.

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## 1. Introduction

Article 5.1 of Council Decision 2005/387/JHA <sup>(1)</sup> (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 February 2016, the EMCDDA and Europol examined the available information on the new psychoactive substance methyl 2-[[1-(cyclohexylmethyl)indole-3-carbonyl]amino]-3,3-dimethylbutanoate, commonly known as MDMB-CHMICA, 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 MDMB-CHMICA satisfied criteria 1, 3, 4, 5, 6. The two agencies therefore concluded that sufficient information had been accumulated to merit the production of a Joint Report on MDMB-CHMICA as stipulated by Article 5.1 of the Council Decision.

## 2. Information collection process

In compliance with the provisions of the Council Decision, on 8 February 2016 the EMCDDA and Europol launched a procedure for the collection of information on MDMB-CHMICA, 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 21 March 2016; additional information and clarifications from some countries were received up to two weeks after this date.

### Information collected by Europol

Europol asked the Europol National Units to provide information on:

- the level of production of MDMB-CHMICA in their country;
- the level of distribution of MDMB-CHMICA in their country;
- the level of trafficking of MDMB-CHMICA in their country, both for internal, transit or export purposes;
- the number of seizures of MDMB-CHMICA 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 MDMB-CHMICA in their country; and,
- any known aspect of violence and/or money laundering relating to the production and trafficking of MDMB-CHMICA.

Europol received responses from 17 Member States <sup>(2)</sup>.

### 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 MDMB-CHMICA has obtained a marketing authorisation;
- the new psychoactive substance MDMB-CHMICA is the subject of an application for a marketing authorisation; and,
- a marketing authorisation that had been granted in respect of the new psychoactive substance MDMB-CHMICA has been suspended.

Twenty-six countries provided a response to the EMA's request regarding human and/or veterinary medicinal products <sup>(3)</sup>. The EMA also provided information as relevant to the centralised procedure for authorising human and veterinary medicinal products.

Furthermore, in anticipation of Article 7.3 of the Council Decision in relation to the manufacturing of medicinal

<sup>(1)</sup> OJ L 127, 20.5.2005, p. 32.

<sup>(2)</sup> Belgium, Croatia, Cyprus, Denmark, Germany, Greece, Finland, France, Hungary, Italy, Latvia, Lithuania, Luxembourg, Portugal, Romania, Spain, and Sweden.

<sup>(3)</sup> Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom provided a response in relation to human and veterinary medicinal products. Malta provided a response in relation to human medicinal products. France, Italy, the Netherlands, and Romania provided a response in relation to veterinary medicinal products.

products in the European Union, the EMA also requested information on whether the new psychoactive substance MDMA-CHMICA 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; and,
- for which a marketing authorisation has been suspended by a competent authority.

Twenty-four countries <sup>(4)</sup> 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:

1. a structured questionnaire to the Reitox National Focal Points. The EMCDDA received replies from 27 Member States <sup>(5)</sup>, as well as Turkey, and Norway;
2. data previously reported to the EMCDDA and Europol through European Union Early Warning System, including EMCDDA–Europol Reporting Forms and Progress Reports and Final Reports;
3. routine monitoring of open source information;
4. a specific information request to the World Health Organization on whether or not MDMA-CHMICA is under assessment by the United Nations system; and,
5. 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 MDMA-CHMICA.

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) <sup>(6)</sup>. The information included in sections 3.8.3 (in part), 4.1, 4.2 and 4.3 was

<sup>(4)</sup> Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Poland, Portugal, Slovenia, Spain, and Sweden provided a response in relation to human and veterinary medicinal products. Malta, Slovakia, and the United Kingdom provided a response in relation to human medicinal products. Italy, the Netherlands, and Romania provided a response in relation to veterinary medicinal products.

<sup>(5)</sup> No reply to the Joint Report Questionnaire request was received from the Netherlands.

<sup>(6)</sup> Parts of the sections on chemistry, pharmacology and toxicology, dependence liability and abuse potential, and characteristics of users is taken from a technical review on MDMA-CHMICA produced under contract from the EMCDDA by Dr Bjoern Moosmann and Dr Volker Auwärter (contract CT.16.SAT.0012.1.0).

provided by the EMA. The conclusion of the Joint Report was prepared and agreed by the EMCDDA and Europol who are the two agencies responsible for the report.

## 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

MDMA-CHMICA (Figure 1) 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.

MDMA-CHMICA has an indole core, which is a common structural feature in many of the synthetic cannabinoids monitored by the EMCDDA such as JWH-018 <sup>(7)</sup>, which is controlled under the United Nations Convention on Psychotropic Substances, 1971.

MDMA-CHMICA possesses one asymmetric carbon atom. The absolute configuration has not been described in the literature.

MDMA-CHMICA was first offered online under the misleading semi-systematic name 'MMB-CHMINACA' and although most of the online shops continue to offer this substance under the name 'MMB-CHMINACA', which falsely implies an indazole core structure, this name should not be used in the scientific or regulatory literature <sup>(8)</sup>.

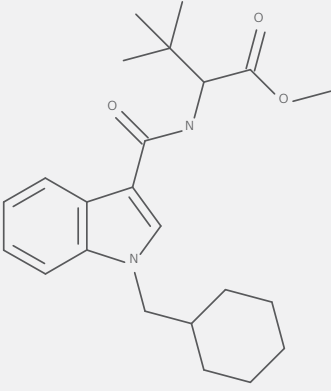
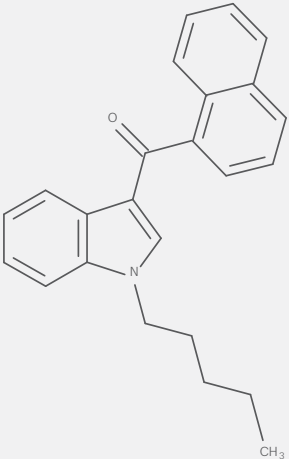
The molecular structure, molecular formula, and molecular mass of MDMA-CHMICA are provided in Figure 1.

<sup>(7)</sup> Systematic name: naphthalene-1-yl(1-pentyl-1H-indol-3-yl)methanone.

<sup>(8)</sup> Different naming systems exist and are utilized for applying short/code names to synthetic cannabinoids and therefore inconsistencies between such systems can lead to erroneous and misleading short names, as seen here with the use of MMB-CHMINACA.

FIGURE 1.

**Molecular structure, molecular formula, and molecular mass of MDMB-CHMICA. Information on JWH-018 is provided for comparison**

		
	MDMB-CHMICA	JWH-018
Molecular formula	C <sub>23</sub> H <sub>32</sub> N <sub>2</sub> O <sub>3</sub>	C <sub>24</sub> H <sub>23</sub> NO
Molecular mass	384.5178	341.45

*Commonly used names:* MDMB-CHMICA

*Systematic (IUPAC) name:* methyl 2-[[1-(cyclohexylmethyl)indole-3-carbonyl]amino]-3,3-dimethylbutanoate

*Other chemical names:* methyl 2-([1-(cyclohexylmethyl)-1H-indol-3-yl]carbonyl)amino-3,3-dimethylbutanoate; methyl 2-[[1-(cyclohexylmethyl)-1H-indol-3-yl]formamido]-3,3-dimethylbutanoate; methyl N-[[1-(cyclohexylmethyl)-1H-indol-3-yl]carbonyl]-3-methylvalinate; N-(1-methoxy-3,3-dimethyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1H-indole-3-carboxamide <sup>(9)</sup>

*Other names and code names:* MMB-CHMINACA

Chemical Abstracts Service (CAS) registry numbers: 1863065-84-2 <sup>(10)</sup>

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

<sup>(9)</sup> This systematic name has been used in the legislation from the People's Republic of China which placed MDMB-CHMICA under national drug control legislation on 1 October 2015.

<sup>(10)</sup> A different CAS registry number of 1715016-78-6 is reported from some sources on the Internet as well as in the legislation from the People's Republic of China which placed MDMB-CHMICA under national drug control legislation on 1 October 2015.

## Physical description

In its pure form MDMB-CHMICA is an odourless, white crystalline solid. It is soluble up to approximately 20 mg/ml in DMF and 5 mg/ml in DMSO (Cayman, MSDS). The substance is expected to be poorly soluble in water. The melting point is stated to be 133–134°C (Toronto Research Chemicals, MSDS).

## Chemical stability and typical reactions

Storage in solution or under non-ideal conditions (e.g. high humidity or elevated temperatures) can lead to hydrolysis of the carboxylic ester function. Ester hydrolysis was shown to occur during smoking by analysis of smoke condensates (Moosmann and Auwärter, 2016).

## Detection and analysis

The analytical profile of MDMB-CHMICA has been described in a publication utilising NMR, LC-HRMS, IR and UV-VIS detection (Langer et al., 2016). Quantification of MDMB-CHMICA in products can be carried out according to the general procedure described in the UNODC manual 'Recommended methods for the identification and analysis of synthetic cannabinoid receptor agonists in seized materials', e.g. by HPLC-DAD analysis (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. and 3.4.

#### 3.2.1. Information provided to Europol

Europol received replies from 17 Member States (Belgium, Croatia, Cyprus, Denmark, Finland, France, Germany, Greece, Hungary, Italy, Latvia, Lithuania, Luxembourg, Portugal, Romania, Spain, and Sweden).

The majority of countries who provided information to Europol reported that the information they had on MDMB-CHMICA was very limited. Belgium, Croatia, Italy and Portugal reported that they had no information on MDMB-CHMICA.

Four Member States (Germany, Hungary, Romania, and Sweden) provided more detailed information in relation to the distribution, trafficking and illicit production/processing aspects.

#### The level of production

Hungary and Romania indicated that criminal syndicates operating in their countries are responsible for tableting and/or processing sites (mixing, packaging), where NPS imported from China are prepared for a final distribution (via the Internet and/or shipping companies).

Germany provided details on an investigation that led to the dismantling of a processing site, where herbal mixtures with MDMB-CHMICA were prepared. Tablets mimicking ecstasy but containing different NPS were also detected. In November 2015 German police seized a total quantity of 17.7 kilogram of NPS herbal mixtures during a house search. Moreover, several small plastic bags contained different powders and tablets were found and seized and all the necessary ingredients required for tableting were found: caffeine, other binding agents, coloured substances, vitamin preparations and packaging units. It was stated from an individual involved in the processing that he mixed the herbal material with the synthetic cannabinoid "MMB-CHMINACA" (MDMB-CHMICA) and then sold the mixtures via the internet.

Forensic analysis conducted as part of this investigation resulted in the following findings, specifically in relation to MDMB-CHMICA <sup>(1)</sup>:

- 365.62 gram of herbal mixture: MDMB-CHMICA
- 9 612 gram of herbal mixture: MDMB-CHMICA and ADB-CHMINACA.

#### The level of distribution

In excess of 2100 small and bulk <sup>(12)</sup> seizure amounts were reported to Europol: Cyprus (6 seizures), Denmark (2), Finland (10), France (2), Germany (over 100), Greece (2), Hungary (1257), Spain (1), Latvia (2), Lithuania (46), Luxembourg (2), Romania (409) and Sweden (334).

##### *Cyprus*

Cyprus recorded 6 seizures of MDMB-CHMICA in 2015. In total 58 g of herbal material (green colour) containing MDMB-CHMICA was seized.

##### *Denmark*

Denmark reported that 2 seizures of MDMB-CHMICA have taken place since December 2014. Both were seizures of plant material (3.1 g and 52.7 g) (SPICE) sprayed with MDMB-CHMICA. Danish authorities stated that substance was purchased via the Internet (non-Danish websites) and then shipped to Denmark by mail.

##### *Finland*

Finland reported 10 seizures of MDMB-CHMICA were recorded in 2015, mostly as postal deliveries at Helsinki airport. In total approximately 50 g of MDMB-CHMICA was seized.

##### *France*

France reported 2 minor seizures of MDMB-CHMICA in 2015 conducted by French Customs. Both seizures were post parcels, the first contained less than 1 g of MDMB-CHMICA mixed with 5F-AKB48 and the second 12 g. No seizures were made in 2014.

##### *Germany*

Germany brought attention to an important issue, which could have an effect on the total number of MDMB-CHMICA seizures reported. In late 2014, early 2015 it was considered that MDMB-CHMICA and MMB-CHMINACA were the same substances. Afterwards it was clarified that they are not. In general it is assumed that all seizures or information received in relation to the MMB-CHMINACA are rather MDMB-CHMICA

<sup>(1)</sup> Other NPS were also detected as part of this investigation into a processing site in Germany, including: synthetic cathinones i.e. 4-CMC, buphedrone; arylalkylamines i.e. EAPB; and other synthetic cannabinoids i.e. ADB-CHMINACA.

<sup>(12)</sup> In this context, 'bulk seizure' is defined as a single seizure in excess of 1 kg.

and in these cases MDMA-CHMICA was labelled as MMB-CHMINACA just by mistake.

According to German authorities approximately hundreds of seizure cases associated with MDMA-CHMICA have been recorded. In the majority of these cases MDMA-CHMICA was seized in small quantities from 0.1 g to 3.8 g. MDMA-CHMICA was seized both as an ingredient in so called herbal mixtures and also as pure substance.

Germany provided more specific details on seizures related MDMA-CHMICA:

1. Seizure of 682.41 g of herbal mixture labelled as 'Damiana 1kg herbal accelerator' in March 2015. Forensic analysis revealed the following composition: AB-CHMINACA, 5F-NPB-22, and MDMA-CHMICA.
2. Seizure of 975 g of herbal mixture accompanied by a seizure of 3 429 g in different packages of herbal mixtures (from 1g to 5 g) on 7 December 2015. Results of the forensic analysis confirmed that MDMA-CHMICA was the only active substance.
3. Seizure of a total of 9 612 g of herbal mixtures with MDMA-CHMICA and AB-CHMINACA and 365.62 g of herbal mixture with MDMA-CHMICA in November 2015 <sup>(13)</sup>.

Germany reported that cases associated with MDMA-CHMICA show that this NPS is well known among drug users and is quite often offered either by drug dealers or via internet.

In addition to 9 deaths associated with MDMA-CHMICA, German authorities recorded 34 non-fatal intoxications cases involving 43 persons. These incidents occurred between September 2014 and October 2015. The persons concerned were between 13 to 39 years old, most between 16 to 31 years. 32 of them had to be hospitalized. In 22 cases the persons concerned had smoked a herbal mixture (e.g. Manga Hot, Cloud Nine, Mad Hatter, Bubblegum). Five of them consumed MDMA-CHMICA as a powder. In the other cases there is no data available concerning the consumption.

The users suffered from nausea, dyspnoea, and tachycardia, inability to move and syncope as well as psychological problems such as disorientation, confusion, acute psychoses, hallucinations and delusions. In 4 cases the users were reported to have been in a critical condition.

In addition, in January 2016 a traffic accident occurred in Seelze. The accident perpetrator (26 years old, male) could not remember what was happening. His pronunciation was unclear and highly slowed. Inside his bag an open package of the herbal mixture "Mr. Nice Guy Second Generation" was

found and seized. The forensic analyses of the remainder of the mixture resulted 5F-ADB. The blood analyses identified five synthetic cannabinoids: AB-CHMINACA, AB-FUBINACA, 5F-PB-22, MDMA-CHMICA, and ADB-CHMINACA.

Furthermore, German police received information from a German jail that numerous prisoners (that were drug users) had collapsed, vomited, had muscle spasms and required hospitalisation. Checks confirmed that the prisoners received inconspicuous letters with normal writing paper laced with synthetic cannabinoids. The prisoners cut the writing paper into pieces and smoked them mixed with tobacco. One unit of consumption is about a 2x2 cm piece of paper. The forensic analyses identified presence of the following the synthetic cannabinoids: MDMA-CHMICA, AB-CHMINACA, ADB-CHMINACA, AM-2201, AB-FUBINACA and ADB-FUBINACA.

#### *Greece*

Greece reported 2 seizures of MDMA-CHMICA. In the first case 0.6 g herbal mixture containing MDMA-CHMICA was seized by the Security Department of Drapetsona. In a second case the Security Department of Libadeia seized 56 small plastic packages that contained herbal mixture with MDMA-CHMICA. A possible country of origin was indicated as Albania.

#### *Hungary*

Hungary formally reported the first seizure of MDMA-CHMICA via the EU EWS on 12 September 2014. The notification was based on the detection of MDMA-CHMICA in a green/brown herbal product of 0.19g seized by Hungarian Police in Ács in August 2014.

The presence of MDMA-CHMICA was confirmed in 715 seizures recorded in 2014 and in 542 in 2015. There have been 19 seizure of the substance in the powder form with total amount of 225 g and 1178 seizures of herbal material with total amount of 5.01 kg. In 31 % of all reported seizures the substance was mixed with other compounds. The other NPSs frequently mixed together with MDMA-CHMICA were, for instance 5F-AMBICA (10 % of the seizures), 5F-AMB (5 % of the seizures) and AB-CHMINACA (4 % of the seizures). The purity of powder samples in 5 cases analysed by forensic analysis revealed very high concentrations of 95 % or more. The concentration of the MDMA-CHMICA in herbal mixture was identified at being from 1 to 8 %.

In the majority of cases the MDMA-CHMICA was sent from China and, to a lesser extent, the United Kingdom. Air cargo shipments or mail orders were often used through Budapest Ferenc Liszt International Airport. In the course of investigation an important link was identified with a company based in the United Kingdom that provided different NPS, including MDMA-CHMICA to Hungary.

<sup>(13)</sup> This seizure information is the same as that reported in the German processing site detected in 2015 – see section on 'The level of production'.

*Latvia*

Latvia reported 1 postal seizure recorded in 2015. The parcel arrived from the United Kingdom. In total 6.0814 g of herbal mixture was seized containing MDMA-CHMICA and 5F-AKB48. In another case Latvian authorities seized 115.6262 g MDMA-CHMICA as herbal mixture.

*Lithuania*

Lithuanian authorities recorded 46 seizures of MDMA-CHMICA in 2015, with a total amount of 4 kg 405 g. The largest single seizure was 4 kg, with purity of 0.2 %.

*Luxembourg*

In Luxembourg there have also been two seizures recorded in 2014 and 2015 one of which is the biggest single seizure of this substance reported in the EU. The biggest seizure was reported in 2014 and was seized in freight cargo from China (Shanghai) and was destined for Spain (Madrid). In total 40 kg of MDMA-CHMICA in powder form was seized.

The second minor seizure was recorded in 2015, when during a music festival 1.2 g of herbal mixture with traces of MDMA-CHMICA was seized (country of origin is unknown).

*Romania*

Romania reported this substance via the EWS to the EMCDDA in November 2014 for the first time. In 2015 409 seizures of MDMA – CHMICA have been registered, with a total amount of 9 423.005 grams. Intelligence revealed that in the majority of cases the substance was imported from China. In one particular case investigated by the Romanian authorities, a criminal group imported NPS from China to Romania via the Czech Republic and Hungary.

Members of this criminal organisation were Hungarian nationals with Croatian origin.

Romanian authorities also underlined significant problems with the identification of this particular NPS in all overdose/hospitalised cases in Romania, due to the lack of a proper identification tool. Therefore, no links have been found between MDMA-CHMICA as a contributing compound to registered overdoses cases in Romania.

As it was stated the substance was imported from China via internet and then distributed via different countries. During investigations two websites were identified as facilitators to order this NPS.

*Spain*

Spain reported 1 seizure of MDMA-CHMICA in 2015, in the framework of a law enforcement operation. In total 4.8 kg of the substance were seized and four persons (Italian citizens) were arrested. It was reported that Spain was not a final

destination for this shipment, but other unspecified Member States.

*Sweden*

Sweden reported the following seizure data recorded by Swedish law enforcement agencies:

- 173 seizures in 2014 (154 seizures were analysed in 2014)
- 159 seizures in 2015 (187 seizures were analysed in 2015)
- 2 seizures in 2016 (4 seizures were analysed in 2016).

The total amount of this seizures was 1 637 gram analysed in 2014, 1 740 gram analysed in 2015 and 192 gram analysed in 2016. The total amount of seizures from January 2014 until beginning of February of 2016 was 3 570 grams.

In addition, Sweden reported that MDMA-CHMICA has been sold on the internet. As for spice in general, the spread of this substance has been seen all over the country with some concentration to certain parts, mostly smaller cities. There have also been a few cases recorded in Stockholm. After scheduling of this substance there have been no internet sales at Swedish marketplace. The most common users identified for this substance are men born in the 1990's.

### 3.2.2. Information provided to the EMCDDA

The EMCDDA received responses from 27 Member States, as well as from Turkey and Norway. Of these, 19 Member States (Austria, Belgium, Bulgaria, Croatia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Latvia, Lithuania, Luxembourg, Poland, Romania, Sweden, Slovakia and the United Kingdom), Turkey, and Norway reported detections of MDMA-CHMICA <sup>(14)</sup>.

#### Seizures

Overall, in excess of 3 600 seizures <sup>(15)</sup> were reported to the EMCDDA by 19 Member States, Turkey, and Norway: Austria (20 seizures), Belgium (2), Bulgaria (16), Croatia (33), Denmark (4), Estonia (15), Finland (53), France (5), Germany (1), Greece (3), Hungary (1405), Latvia (10), Lithuania (52), Luxembourg (2), Poland (223), Romania (2), Sweden (521),

<sup>(14)</sup> '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.)

<sup>(15)</sup> Many 'seizures' relate to individual case-level data, however, some data provided to the EMCDDA are aggregated at the country level. Data is drawn from the Joint Report Questionnaires and data provided in the bi-annual data gathering (EU EWS Progress Reports and Final Reports) and from individual EMCDDA–Europol Reporting forms submitted to the EMCDDA on an ad hoc basis.



Slovakia (3), the United Kingdom (550), Turkey (656), and Norway (9).

MDMA-CHMICA has typically been seized as herbal material. Over 90 % of seizures reported by countries where MDMA-CHMICA has been detected have been of herbal material. This includes the seizure of a large number of branded 'legal high' smoking mixtures. Over 98 kg of MDMA-CHMICA has been seized, almost 54 kg of which was seized as herbal material and almost 43 kg seized in powder form. In the remaining amount seized, the physical form of MDMA-CHMICA was undefined.

The largest single bulk seizure reported to the EMCDDA was 40 kg of MDMA-CHMICA in powder form by Luxembourg, in December of 2014. The powder was contained in 1 kg packages and was seized at Luxembourg airport where it was in transit from China (Shanghai) with Spain (Madrid) as the final destination.

Seizures in excess of 1 kg were reported by 7 countries: Hungary (6.8 kg), Latvia (1.2 kg), Luxembourg (40 kg), Romania (2.9 kg), Sweden (4.9 kg), Turkey (34.8 kg) and the United Kingdom (5.9 kg).

Where MDMA-CHMICA has been detected with other substances, it has almost exclusively been detected in combination with other synthetic cannabinoids such as: 5F-AMB (5F-AMB-PINACA), 5F-AMBICA, AB-CHMINACA, 5F-AKB48, 5F-AMB-PINACA, and AB-FUBINACA.

### Collected samples

A total of 4 Member States reported 60 samples that contained MDMA-CHMICA collected from users and from bricks-and-mortar shops and online shops: Spain (3), France (2), Slovenia (2), and the United Kingdom (53). Some of these collected samples were linked to biological detections including serious adverse events.

The first collected sample was reported by the United Kingdom in September 2014 and was a sample mislabelled as MMB-CHMINACA. The most recently reported collected sample was also reported by the United Kingdom in February 2016.

### Biological samples

A total of 306 detections where MDMA-CHMICA was analytically confirmed in biological samples were reported by 7 Member States (Austria, Germany, Estonia, Hungary, Poland, Sweden and the United Kingdom) and Norway.

These related to:

- 53 serious adverse events (25 acute intoxications and 28 deaths);

- 10 cases related to intoxications reported to the Poisons Information Centre (aggregated data, details not specified);
- 135 cases reported as aggregated data associated with forensic case work (details not specified);
- 8 cases of persons suspected of driving under the influence of drugs (including 1 traffic accident);
- 100 cases related to unlawful activity (which included driving under influence of drugs/alcohol, underage drinking, violent public behaviour, or suspicion of drug consumption).

### 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 detailed information concerning the involvement of organised crime in the manufacture and/or trafficking of MDMA-CHMICA was provided by any of reporting states.

#### The level of trafficking

No detailed information concerning the involvement of organised crime in the manufacture and/or trafficking of MDMA-CHMICA was provided by any of reporting states.

However, 3 Member States (Germany, Hungary, and Romania) referred to an involvement of the criminal groups in whole chain of the NPS trade (from importation to final distribution).

German authorities stated that no direct links with organised crime groups (OCG) have been identified. However, easy access to the MDMA-CHMICA in smaller amounts via Internet-shops in and outside of the EU, as well as in bigger amounts via Internet trade boards mostly from wholesalers in China or other Asian countries indicate at least a certain degree of organisation.

Hungary and Romania highlighted that criminal syndicates that operate in their countries are responsible for setting up tableting and/or processing sites (mixing, packaging), where NPS imported from China are prepared for final distribution (via Internet and/or shipping companies).

#### Money laundering aspects

No specific information was received on money laundering phenomenon, in relation to the production and/or trafficking of MDMA-CHMICA.

Romania however reported the incomes generated by criminal groups that deal with NPS are used to purchase real estates and vehicles. During a few investigations conducted by the Romanian authorities those types of goods purchased by criminal syndicates for money derived from criminal activities were identified and seized.

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

No information was reported in respect to violence in connection with production, wholesale and distribution of MDMA-CHMICA.

### 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. Serious adverse events reported to the EMCDDA

Case-level data for 71 serious adverse events<sup>(16)</sup> associated with MDMA-CHMICA were reported to the EMCDDA by 8 Member States (Austria, France, Germany, Hungary, Poland, Spain, Sweden, and the United Kingdom) and Norway. These cases comprised 42 acute intoxications and 29 deaths; they occurred between 2014 and 2016<sup>(17)</sup>.

#### Acute intoxications

Case-level data for 42 acute intoxications associated with MDMA-CHMICA were reported by 7 countries: Austria (7 cases), France (2), Germany (7), Poland (3), Spain (2), Sweden (10) and the United Kingdom (11).

For 35 of these cases, analytical confirmation of consumption of MDMA-CHMICA was obtained from biological samples (25 cases) or from epidemiologically linked samples (products either used or presumed to have been used by the patients) (10 cases). The remaining 7 cases (3 cases from Poland and 4 cases from Sweden) were excluded from further analysis because MDMA-CHMICA was not analytically confirmed from either a biological sample or an epidemiologically linked sample.

<sup>(16)</sup> Serious adverse event means any adverse event, whether analytically confirmed or not, that is associated with the consumption of a new psychoactive substance in a human that: results in death; is life-threatening; requires intensive treatment in an emergency room and/or requires hospitalisation; results in persistent or significant disability or incapacity; results in substance dependency or substance abuse; consists of a congenital anomaly or birth defect; or is an important medical event that may not be immediately life-threatening or result in death or hospitalisation but may jeopardise the patient or may require intervention to prevent one of the other outcomes listed above. Examples of such events are: convulsions that do not result in hospitalisation.

<sup>(17)</sup> Europol received reports of 34 acute intoxications and 9 deaths associated with MDMA-CHMICA occurring in Germany between September 2014 and October 2015. Some of these reports may be duplicates with the data reported to the EMCDDA. However, given the strict deadlines imposed by the Council Decision 2005/387/JHA it had not been possible to ascertain this at the time of writing the Joint Report. As a result, the analysis below refers to the 71 serious adverse events reported to the EMCDDA.

The large majority of 35 cases appear to have been treated in hospital emergency departments. All the cases occurred during 2014 and 2015. In 19 out of 35 cases the individuals recovered; for the remaining 16 cases the outcome of the intoxication was unknown or not reported.

In 3 of the 25 acute intoxications that were analytically confirmed from biological samples, MDMA-CHMICA was the only substance identified. In the remaining 22 cases MDMA-CHMICA was detected along with other substances. These were typically other cannabinoids (including THC and its metabolites) and ethanol. Other substances detected included benzodiazepines, morphine, and buprenorphine.

#### Demographics

26 (74 %) of the acute intoxications were male; 7 (20 %) were female; in 2 (6 %) cases the gender of the patient was unknown. The mean age of the male cases for which an age was known was 25 years (median 22); for the female cases for which an age was known, the mean age was 27 years (median 20). For all cases, the ages ranged between 15 and 50 years old.

#### Clinical symptoms

Data on the clinical symptoms<sup>(18)</sup> related to the 3 intoxications where MDMA-CHMICA was the only substance detected were generally consistent with those associated with intoxication by synthetic cannabinoids previously reported in the literature (Tait et al., 2016). These included: confusion, aggression, changes in mood, hallucinations, dilated pupils, hyperemesis, and unresponsiveness.

For the remaining 32 cases, the reported symptoms were also generally consistent with the symptoms associated with intoxication by synthetic cannabinoids (Tait et al., 2016). These included: unconsciousness or coma (12 cases), hyperemesis and/or nausea (6), seizures and convulsions (5), tachycardia (5), bradycardia (2), mydriasis (3), syncope (2), spontaneous urinating and defecating (2), shortness of breath (2), somnolence (2), respiratory acidosis (1) metabolic acidosis (1), collapse (1), lower limbs paralysis (1), and chest pain (1).

Aggression and/or severe disturbance of behaviour were reported in at least 6 cases, some of which resulted in police intervention and transfers to psychiatric units.

<sup>(18)</sup> Includes abnormal laboratory findings.

#### Route of administration

In 21 cases the route of administration was reported to be smoking or inhalation.

#### Physical form

In 18 cases the physical form of MDMA-CHMICA used by the patients was reported to be herbal material. In two cases the herbal material containing MDMA-CHMICA was mixed with another synthetic cannabinoid as a powder.

#### Amount or dose administered

No information was reported on the amount of MDMA-CHMICA used by the patients. In one case the serious adverse effects were felt after smoking '1 joint'; in another the patient felt the adverse effects after '2 or 3 inhalations'.

#### Deaths

Case-level data for 29 deaths associated with MDMA-CHMICA were reported by 5 Member States and Norway: Germany (5 cases), Hungary (3), Poland (1), Sweden (9), the United Kingdom (10), and Norway (1). MDMA-CHMICA was analytically confirmed in biological samples in 28 cases and from an epidemiologically linked sample in 1 case.

#### Demographics

Of the 29 deaths, 25 were male (86 %), 3 were female (10 %), the gender was not reported for one death<sup>(19)</sup>. The decedents' ages ranged from 17 to 52 years old. The mean age of the male decedents was 33 years (median 33); the mean age of the female decedents was 31 years (median 30).

#### Cause of death

The cause of death was reported in 21 cases. For the remaining 8 cases information on the cause of death was not available.

- In 1 case the cause of death was reported to be caused by MDMA-CHMICA;
- In 4 cases the information provided on the cause of death suggested that it was *probably* or *possibly* caused by MDMA-CHMICA;
- In 5 cases MDMA-CHMICA was reported to have contributed to the cause of death;
- In 2 cases the information provided on the cause of death suggested that MDMA-CHMICA *probably* or *possibly* contributed to the cause of death;
- In 2 cases the cause of death was reported as drug overdose or mixed intoxication;
- In 7 cases an alternative cause of death was reported.

<sup>(19)</sup> No gender was reported for one of the cases.

#### Route of administration

In all the 11 fatalities for which a route of administration was reported, MDMA-CHMICA was either smoked (9 cases) or presumed to have been smoked (2).

#### Source

Information on where the decedents had sourced the substance was available in 3 cases: in 2 of them MDMA-CHMICA was sourced from the internet. In the remaining case the substance was supplied by a friend.

#### Amount or dose administered

No information was reported on the amount of substance administered by the decedents.

### 3.4.2. Pharmacology

#### Pharmacodynamics

MDMA-CHMICA is a highly potent full agonist at the CB<sub>1</sub> receptor of the endocannabinoid system. Using a cAMP assay MDMA-CHMICA showed an EC<sub>50</sub> approximately 8 times lower than the EC<sub>50</sub> of JWH-018, and a twofold lower EC<sub>50</sub> than AB-CHMINACA<sup>(20)</sup> (Table 1) (Moosmann and Auwärter, 2016).

The relatively high pharmacological potency is also supported by the data available for other synthetic cannabinoids and from structure-activity relationships (SAR). Frequently, a substitution of the indole core structure with an indazole core leads to a significant reduction of the activity at the CB<sub>1</sub> receptor. This was observed in the case of APICA<sup>(21)</sup> and APINACA<sup>(22)</sup> (IC<sub>50</sub>: 175 nM vs. 824 nM) (Uchiyama et al., 2012) and in the case of AM-2201 and THJ-2201 (EC<sub>50</sub>: 0.45 nM vs. 1.68 nM) (Moosmann and Auwärter, 2016).

TABLE 1

Half maximal effective concentration (EC<sub>50</sub>) and efficacy as compared to the full agonist CP 55,940 (E<sub>max</sub>) of MDMA-CHMICA and other synthetic cannabinoids as assessed using a cAMP assay (CB<sub>1</sub> receptor, DiscoverX) (Moosmann and Auwärter, 2016)

Compound	EC <sub>50</sub> [nM]	E <sub>max</sub>
JWH-018	1.13	97%
MDMA-CHMICA	0.14	94%
AB-CHMINACA	0.27	94%
AB-FUBINACA	0.89	97%

<sup>(20)</sup> Systematic name: N-[(1S)-1-(aminocarbonyl)-2-methylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide.

<sup>(21)</sup> Systematic name: N-(1-adamantyl)-1-pentyl-1H-indole-3-carboxamide.

<sup>(22)</sup> Systematic name: N-(1-adamantyl)-1-pentyl-1H-indazole-3-carboxamide.

Comparing the binding affinity towards the CB<sub>1</sub> receptor and the intrinsic activity of compounds carrying an isopropyl moiety (e.g. AB-CHMINACA) with their respective *tert*-butyl analogues (e.g. ADB-CHMINACA<sup>(23)</sup>), it can be observed that the introduction of a *tert*-butyl moiety typically leads to an increase in affinity and activity of the compounds (e.g. AB-CHMINACA K<sub>i</sub>: 0.519 nM; EC<sub>50</sub>:IC<sub>50</sub> 2.55 nM vs. ADB-CHMINACA K<sub>i</sub>: 0.289 nM; EC<sub>50</sub>:IC<sub>50</sub> 0.62 nM) (Moosmann and Auwärter, 2016).

Furthermore, comparing the CB<sub>1</sub> receptor affinities and activities of carboxamide compounds with their methyl ester analogues, a significant further increase can frequently be observed (e.g. ADB-CHMINACA K<sub>i</sub>: 0.289 nM; EC<sub>50</sub>:IC<sub>50</sub> 0.62 nM vs. MDMA-CHMINACA K<sub>i</sub>: 0.094 nM; EC<sub>50</sub>:IC<sub>50</sub> 0.330 nM) (Bluchler et al., 2011; Buchler et al., 2009; Banister et al., 2015).

Langer and co-workers (Langer et al., 2016) report a K<sub>i</sub> of MDMA-CHMICA at the CB<sub>1</sub>-receptor of 0.09 nM. However, the reference stated by the authors does not contain data on MDMA-CHMICA. Instead, the K<sub>i</sub> of MDMA-CHMINACA is reported there with the same value.

As it has been shown for some of the first synthetic cannabinoids to appear on the drug market (e.g. JWH-018, JWH-073) and for the THC metabolite 11-hydroxy-THC, it is likely that some of the mono-hydroxylated metabolites of MDMA-CHMICA retain activity at the CB<sub>1</sub> receptor and they might therefore contribute to the pharmacological profile of the compound. However, in the case of CB<sub>1</sub> receptor activity, it is unclear if the metabolites are able to cross the blood-brain-barrier and reach effective concentrations levels in the central nervous system. Based on the properties of structurally related compounds like MDMA-CHMINACA or ADB-CHMINACA, the ester cleavage product (a free carboxylic acid) may not show relevant affinity towards the CB<sub>1</sub> receptor (Buchler et al., 2011).

No data regarding the binding affinity or activity towards the CB<sub>2</sub> receptor is available in the literature. In contrast to CB<sub>1</sub> receptors, CB<sub>2</sub> receptors are mainly expressed on cells of the immune system and consequently, if MDMA-CHMICA binds to the CB<sub>2</sub> receptor, modulation of the immune system could be the result.

There are no data available on the effect of MDMA-CHMICA on other pharmacological (receptor or enzyme) targets. The biological properties of its metabolites are also unknown.

## Pharmacokinetics

MDMA-CHMICA undergoes extensive metabolism in the human body. Similar to other synthetic cannabinoids which have been studied it is not excreted unchanged in urine to a relevant extent.

The main metabolic reactions comprise mono-hydroxylations and hydrolysis of the carboxylic ester function. In total, 31 metabolites could be identified *in vivo* (Moosmann and Auwärter, 2016). The four most abundant metabolites detected in human urine samples were products of either mono-hydroxylation of the cyclohexyl moiety or hydrolysis of the carboxylic ester function.

No data on the pharmacokinetics of MDMA-CHMICA is available in the literature.

## Abuse liability and dependence potential

### Abuse liability

Limited information from self-reported user experiences on user websites appear to suggest that MDMA-CHMICA has an abuse potential.

Other synthetic cannabinoids (JWH-018, JWH-073, JWH-200, CP-47,497 and cannabicyclohexanol) have previously been found to have potential for abuse (Järbe et al., 2011; Järbe et al., 2010; Ginsburg et al., 2012; DEA, 2012).

### Dependence potential

No data are available in the literature regarding the dependence potential of MDMA-CHMICA in animals. Studies evaluating the dependence potential of other synthetic cannabinoids (Ginsburg et al., 2012) suggest that JWH-018 and JWH-073 might have some abuse and dependence liability in monkeys due to a short duration of action. In rhesus monkeys, cross-tolerance was observed after 3 days of THC treatment for THC but not for JWH-018 (Hrubá et al., 2012). The greater loss of sensitivity to Δ<sup>9</sup>-THC relative to JWH-018 suggests that differences in CB<sub>1</sub> receptor agonist efficacy are important *in vivo* and might underlie differences in the dependence liability and adverse effects of synthetic cannabinoids versus cannabis.

No data are available from clinical studies on the dependence potential of MDMA-CHMICA. Four cases of withdrawal symptoms following MDMA-CHMICA consumption were reported to the Poison Information Centre in Freiburg, Germany (Moosmann and Auwärter, 2016). The duration and extent of consumption was not reported.

<sup>(23)</sup> Systematic name: N-[1-(aminocarbonyl)-2,2-dimethylpropyl]-1-(cyclohexylmethyl)-1H-indazole-3-carboxamide.

Other synthetic cannabinoids have been previously found to produce withdrawal symptoms<sup>(24)</sup> in humans (Hermanns-Claussen et al., 2013; Hermanns-Claussen et al., 2012).

### 3.4.3. Toxicology

No published data regarding the toxicity of MDMB-CHMICA have been identified.

Data on cytotoxicity and genotoxicity exists for other synthetic cannabinoids (Koller et al., 2013a; Koller et al., 2013b; Koller et al., 2015; Ferk et al., 2016) but transferability of these data to MDMB-CHMICA is very limited as individual compounds can show distinct toxicological profiles.

Data from serious adverse events associated with MDMB-CHMICA are discussed in this section 3.4.1. Based on the data reported, the symptoms presented in cases of intoxication involving MDMB-CHMICA appear to be broadly similar to those found with other synthetic cannabinoids.

### 3.4.4. Characteristics of users

There is limited data on the characteristics of users of MDMB-CHMICA. 'Legal high' smoking mixtures containing MDMB-CHMICA are marketed as 'legal' replacements to cannabis. It is therefore likely that a range of different cannabis users would be interested in these products. Among other groups this will include those who are regularly subjected to drug testing procedures (see section below on *Prevalence of use*). Information provided to Europol suggests that MDMB-CHMICA has also been consumed by prisoners.

Some of the information available on the users of MDMB-CHMICA discussed in this section derives from self-reported user experiences. It is important to note that it is not possible to confirm the specific substance(s) used by those submitting the reports; nor the strength, purity and dose consumed. While this is generically true for user reports of all new psychoactive substances, it is particularly relevant for users of 'legal high' type herbal mixtures containing synthetic cannabinoids, which are widely known to be highly variable in terms of composition and dosage.

It is also important to note that the information provided on user websites and from specific user groups may not

necessarily be representative of other users of MDMB-CHMICA and should be regarded as illustrative only.

### Route of administration, drug regimens and settings of use

MDMB-CHMICA is typically sold as branded 'legal high' smoking mixtures which are usually smoked or otherwise inhaled; use of self-prepared herbal mixtures have also occasionally been reported.

Herbal mixtures containing MDMB-CHMICA can be administered as a 'joint' or using a vaporizer, 'bong' or pipe. Oral consumption of synthetic cannabinoids as powders or tablets has also been described, albeit to a lesser extent. In the case of oral consumption a strong first-pass-effect can be expected.

### Dose, re-dosing

There are no clinical studies on the doses required to produce subjective effects of MDMB-CHMICA. Limited data from self-reported user experiences posted on user websites claim that subjective effects have been noted using doses of 0.05 mg to 0.3 mg.

It is well established that herbal smoking mixtures vary considerably in terms of composition and content of synthetic cannabinoids. In addition, heterogeneity of the distribution of the MDMB-CHMICA within the herbal mixture can result in uneven and high concentrations of the substance on certain parts of the herbal material (so called 'hot pockets') (Moosmann et al., 2015).

Overall, it is reasonable to assume that the vast majority of users have no idea that they are consuming MDMB-CHMICA, nor what dose they are taking, nor will they be able to reliably control the dose they consume.

### Subjective, psychological, and behavioural effects

There are no non-clinical or clinical studies reporting on the psychological and/or behavioural effects of MDMB-CHMICA.

Discussions on user websites suggest that the subjective effects might be similar to those induced by other synthetic cannabinoids. Reported effects are wide ranging and include euphoria, feeling of warmth, spontaneous laughing, visual and auditory hallucinations, as well as severe anxiety and fear/panic, disorientation, vertigo and violent behaviour.

Data from serious adverse events reported to the EMCDDA include reports of serious acute behavioral disturbances in individuals who have been exposed to MDMB-CHMICA.

<sup>(24)</sup> Withdrawal symptoms after cessation of synthetic cannabinoid use described in the literature include: anxiety, unstable mood, crying fits, feeling of inner emptiness, spatial disorientation, hyperacusis, somatic pain, shortness of breath, hyperventilation, intense sweating, and sensations of motor and inner restlessness.

TABLE 2

Online prices of MDMB-CHMICA. Exchange rates used for calculation in €: 1 GBP = 1.30 €, 1 USD = 0.90 €, 1 PLN = 0.23

	1 g	10 g	100 g	1000 g
Number of products	16	20	19	16
Range	8.50 – 23.40	60.00 – 203.40	405 – 770	1 620 – 6 100
Median	13.90	97.50	545	3 600
Mean	14.93	98.43	556	3 505

### Availability, supply, price

#### Online vendors

A search of the product portfolio of 95 online shops selling research chemicals in various countries (Belgium, Czech Republic, Germany, Hungary, The Netherlands, Poland, Spain, Sweden, United Kingdom, Canada, USA, China) was performed. More than one third of the shops (28 shops) listed MDMB-CHMICA on their website, but only two named the compound 'MDMB-CHMICA' (all others named it 'MMB-CHMINACA'). In 6 of these 28 shops the compound was listed as 'out of stock'. Online prices depended on the order quantity and are summarised in Table 2.

It should be noted that MDMB-CHMICA was controlled in China in October 2015. Despite the change in legal status, some online vendors claiming to be based in China still list MDMB-CHMICA on their webpage, although they do not ship the compound anymore (Moosmann and Auwärter, 2016).

#### Prevalence of use

No published data from general population surveys or targeted surveys on the prevalence of use of MDMB-CHMICA were identified.

The EU 'SPICE' project<sup>(25)</sup> reported that in 2015, 186 samples of synthetic cannabinoids that were test purchased (44 % of all analysed 'herbal mixtures') contained MDMB-CHMICA (Moosmann and Auwärter, 2016). This appears to suggest that in 2015 MDMB-CHMICA was commonly found in 'legal high' smoking mixtures being sold on the market, even though the representatively of the samples analysed cannot be commented on.

An analysis of all the serum and urine analysis conducted at the Institute of Forensic Medicine in Freiburg (Germany) (n=1,377 samples) suggests that MDMB-CHMICA was the

most prevalent synthetic cannabinoid in Germany in 2015. The substance was detected in 54 % (n=205) of all serum samples positive for synthetic cannabinoids (n=1,377) (Moosmann and Auwärter, 2016).

'Legal high' smoking mixtures containing MDMB-CHMICA are marketed as 'legal' replacements to cannabis. It is therefore likely that a range of different cannabis users would be interested in these products. Among others, this would include those subjected to regular drug testing (such as those tested for drug abstinence in the context of drug treatment centres, workplace testing, driving licence re-granting candidates, etc.). Avoidance of drug testing was considered to be a relevant motivation for the use of synthetic cannabinoids by a study who surveyed adults (from 13 different countries) reporting at least one (lifetime) use of synthetic cannabinoids (Vandrey et al., 2012).

Information on the use of MDMB-CHMICA can also be ascertained from discussions on user websites<sup>(26,27)</sup>, despite the (already discussed) limitations of this type of data. From these discussions, it appears that MDMB-CHMICA is also used by psychonauts and users with experience of other synthetic cannabinoids.

### 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 9 February

<sup>(25)</sup> EU funded research project (2010–12), continued by the 'Spice II Plus' project aimed at ensuring a scientific knowledge base (including analytical libraries) on synthetic cannabinoids and other new psychoactive substances (<http://polis.osce.org/library/f/4276/4274/OSCE-BIH-EVT-4276-EN-4274.pdf>)

<sup>(26)</sup> [www.erowid.org/experiences/exp.php?ID=105904](http://www.erowid.org/experiences/exp.php?ID=105904)

<sup>(27)</sup> [www.bluelight.org/vb/threads/735246-New-cannabinoid-MMB-CHMINACA?highlight=MDMB-CHMICA](http://www.bluelight.org/vb/threads/735246-New-cannabinoid-MMB-CHMINACA?highlight=MDMB-CHMICA)

2016, the World Health Organization informed the EMCDDA that MDMB-CHMICA is currently not under assessment and has not been under assessment by the UN system.

### 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 MDMB-CHMICA dates from September 2014 from the Hungarian National Focal Point. The Reporting Form details a seizure of 0.19 g of green/brown herbal product that was seized in August 2014 by Hungarian Police in Ács, Hungary. The identification and analytical characterisation was based on Gas Chromatography-Mass Spectrometry (GC-MS) and Fourier transform infrared spectroscopy (FT-IR) and Nuclear Magnetic Resonance (NMR).

MDMB-CHMICA was added to the list of new psychoactive substances monitored by the EMCDDA and Europol through the European Union Early Warning System and a profile of the substance was created on the European Database on New Drugs (EDND). Since then, analytical details and other information, including public health alerts, 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)

Ten Member States (Croatia, Denmark, Estonia, Finland, Germany, Greece, Hungary, Latvia, Lithuania, and Luxembourg) and Turkey reported that MDMB-CHMICA is controlled under drug control legislation.

- In Croatia, MDMB-CHMICA is part of the list of drugs, psychoactive substances and plants used for drug production, as well as precursors (OG 10/16). MDMB-CHMICA is covered with generic definition 'JWH-018 and its structural analogues'.
- In Denmark, MDMB-CHMICA is controlled under drug control legislation.
- In Estonia, MDMB-CHMICA has been added to drug control legislation since 8 June 2015.
- In Finland, MDMB-CHMICA has been added to drug control legislation since 28 September 2015.
- In Germany, by adoption of the 30th Amending Regulation on Narcotic Drugs (30. Betäubungsmittelrechts-

Änderungsverordnung, BtMÄndV) MDMB-CHMICA is controlled under schedule I (narcotics not eligible for trade and medical prescription) of the German Narcotics Act (Betäubungsmittelgesetz, BtMG). The legislation has been published on November 11th 2015 in the Federal Gazette, and entered into force on 21 November 2015.

- In Greece, MDMB-CHMICA is classified as an isomer of Zipeprol<sup>(28)</sup>. Zipeprol and its isomers are classified in the Table C of the Law 4139/2013.
- In Hungary, MDMB-CHMICA is under drug control legislation from 22/07/2015 through Government Decree 66/2012 (IV. 2).
- In Latvia, MDMB-CHMICA is included in the first list of the Cabinet Regulation N 847 'Regulations regarding Narcotic Substances, Psychotropic Substances and Precursors to be Controlled in Latvia' and the law 'On the Procedures for the Coming into force and Application of the Criminal Law'. Control of MDMB-CHMICA is introduced by the generic approach.
- In Lithuania, MDMB-CHMICA has been placed under control, according to the Republic of Lithuania Minister of Health Order No V-1062 (21/09/2015) 'On the amendment of the Ministry of Health of the Republic of Lithuania Order No. 5 of 6 January 2000.
- In Luxembourg, MDMB-CHMICA is controlled by the Grand Ducale Decree of 04/05/2009.
- In Turkey, MDMB-CHMICA is under legal control via the Generic Classification which was deliberated by the council of Ministers on 26/01/2015 and published in the official gazette on 6 February 2015 the annexed list subject to the provisions of the Law on Control of Drugs numbered 2313; according to the 19th article of the said Law. Generic Classification text is updated and adopted to the said law on 16/02/2016 by the council of Ministers.

Two Member States (Austria and Poland) reported that MDMB-CHMICA is controlled under specific new psychoactive substances control legislation.

- In Austria, MDMB-CHMICA is controlled under the Austrian Act on new psychoactive substances (Neue-Psychoaktive-Substanzen-Gesetz, NPSG).
- In Poland, MDMB-CHMICA is controlled according to the general definition of 'substitute drug' which has been included to the Act of 8 October 2010 amending the Act on counteracting drug addiction and the Act on State Sanitary Inspection (Journal of Laws 'Dz.U.' No. 213, item 1396). Article 44b of the above mentioned Act bans manufacturing or introducing substitute drugs to trade.

One Member State (Sweden) and Norway reported that MDMB-CHMICA is controlled under other types of legislation:

<sup>(28)</sup> Systematic name: 1- methoxy-3-[4- β –methoxyphenethyl]-piperazin-1-yl]-1-phenylpropan-2-ol

- In Sweden, MDMA-CHMICA is controlled Act on the Prohibition of Certain Goods Dangerous to Health (SFS 1999:42).
- In Norway, the import of and trade in MDMA-CHMICA is controlled by Medicinal Products Legislation.

Fourteen Member States (Belgium, Bulgaria, Czech Republic<sup>(29)</sup>, France, Hungary, Italy, Ireland, Malta, Portugal, Romania, Slovakia, Slovenia, Spain, and the United Kingdom) reported that MDMA-CHMICA is not subject to control measures at the national level.

### 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 MDMA-CHMICA which has been detected within Europe.

The synthesis of MDMA-CHMICA may be carried out in analogy to the synthesis of the indazole analogue MDMA-CHMINACA, which has been described previously in a patent application (Buchler et al., 2011; Buchler et al., 2009). It is also possible that MDMA-CHMICA can be synthesised using synthesis routes for similar compounds as described by Banister and colleagues (Banister et al., 2015) and by Adam and colleagues (Adam et al., 2010).

Possible synthetic routes for the production of MDMA-CHMICA could utilise L-tert-leucine methyl ester (for the synthesis of the (S) enantiomer), indole-3-carboxylic acid, indole-3-carboxylic acid methyl ester, indole and cyclohexylmethyl bromide, as potential precursors.

#### 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 MDMA-CHMICA. 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 any Member State that indicated that MDMA-CHMICA had any other use apart from in analytical reference materials and scientific research.

From the available information, it does not appear that MDMA-CHMICA 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 European Union database on the synthetic route of all medicinal products.

In addition, the EMA reported that it is not known if MDMA-CHMICA is used in the manufacture of medicinal products for human or veterinary use and which are centrally authorised within the European Union.

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

### 4.1. Marketing authorization

Twenty two countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Malta, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom) reported that MDMA-CHMICA has not been granted a marketing authorization as a medicinal product for human use. Twenty five countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom) reported that MDMA-CHMICA has not been granted a marketing authorization as a medicinal product for veterinary use.

The EMA also reported that MDMA-CHMICA has not been granted a marketing authorization as a medicinal product for neither human nor veterinary use through the centralized procedure.

<sup>(29)</sup> The Czech Republic reported that an amendment of the Government Regulation No. 463/2013 Coll., on the lists of addictive substances is currently being prepared. MDMA-CHMICA is one of the 33 substances proposed to place under control.



## 4.2. Application for a marketing authorization

Twenty two countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Malta, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom) reported that MDMB-CHMICA is not the subject of an application for a marketing authorization as a medicinal product for human use.

Twenty five countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom) reported that MDMB-CHMICA is not the subject of an application for a marketing authorization as a medicinal product for veterinary use.

The EMA also reported that MDMB-CHMICA is not the subject of an application for a marketing authorization for neither human nor veterinary use through the centralized procedure.

## 4.3. Suspended marketing authorization

Twenty two countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Malta, Norway, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom) reported that that there had been no cases of suspended marketing authorization granted in respect to MDMB-CHMICA as a human medicine.

Twenty five countries (Austria, Belgium, Croatia, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom) reported that that there had been no cases of suspended marketing authorization granted in respect to MDMB-CHMICA as a veterinary medicine.

The EMA also reported that MDMB-CHMICA is not the subject of a suspended marketing authorization for neither human nor veterinary use through the centralized procedure.

## 5. Conclusion

MDMB-CHMICA is a highly potent full agonist at the CB<sub>1</sub> receptor of the endocannabinoid system. While it shares some pharmacological similarities with Δ<sup>9</sup>-tetrahydrocannabinol (THC), which is responsible for the major psychoactive effects of cannabis, laboratory studies suggest that it is much more potent. Overall, very little is known about the pharmacology of MDMB-CHMICA, including its effects on other physiological systems.

MDMB-CHMICA has been available on the European drug market since at least 2014. It has been detected in 19 Member States, Turkey, and Norway. More than 3 600 seizures have been made, which includes 43 kg of powder and 54 kg of herbal material which has been laced with MDMB-CHMICA. This herbal material is typically sold as branded 'legal high' smoking mixtures in head shops as well as on the Internet; 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.

Information reported to Europol and the EMCDDA suggests that bulk powders of MDMB-CHMICA are imported from chemical companies based in China. These powders are then used to produce smoking mixtures within Europe. A large number of products have been detected on the market. Of note is that MDMB-CHMICA was controlled in China in October 2015 which might reduce the availability of bulk powders in Europe.

To date, 71 serious adverse events associated with MDMB-CHMICA have been reported by 8 Member States. This includes serious acute intoxications requiring hospitalisation and 29 deaths; in at least 12 cases MDMB-CHMICA appeared to play a role in the death.

We conclude that the health and social risks caused by the manufacture, trafficking and use of MDMB-CHMICA, 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.

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**Recommended citation:**

European Monitoring Centre for Drugs and Drug Addiction (2016), *EMCDDA–Europol Joint Report on a new psychoactive substance: methyl 2-[[1-(cyclohexylmethyl)indole-3-carbonyl]amino]-3,3-dimethylbutanoate (MDMB-CHMICA)*, Joint Reports, Publications Office of the European Union, Luxembourg.

The Joint Report was submitted to the EU institutions on 14 April 2016. It is published in the original version that has not been edited.

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Luxembourg: Publications Office of the European Union  
doi:10.2810/08132 | ISBN 978-92-9168-925-5

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