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# CUMYL-4CN-BINACA

EMCDDA–Europol Joint Report on a new psychoactive substance: 1-(4-cyanobutyl)-*N*-(2-phenylpropan-2-yl) indazole-3-carboxamide (CUMYL-4CN-BINACA)

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.

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- 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;
- the United States Drug Enforcement Administration.

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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 March 2017, the EMCDDA and Europol examined the available information on the new psychoactive substance 1-(4-cyanobutyl)-*N*-(2-phenylpropan-2-yl)indazole-3-carboxamide, commonly known as CUMYL-4CN-BINACA, 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 CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA, 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.

### Information collected by Europol

Europol asked the Europol National Units to provide information on:

- the level of production of CUMYL-4CN-BINACA in their country;
- the level of distribution of CUMYL-4CN-BINACA in their country;
- the level of trafficking of CUMYL-4CN-BINACA in their country, both for internal, transit or export purposes;
- the number of seizures of CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA in their country;
- any known aspect of violence and/or money laundering relating to the production and trafficking of CUMYL-4CN-BINACA.

Europol received responses from 16 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 CUMYL-4CN-BINACA has obtained a marketing authorisation;
- the new psychoactive substance CUMYL-4CN-BINACA is the subject of an application for a marketing authorisation;
- a marketing authorisation that had been granted in respect of the new psychoactive substance CUMYL-4CN-BINACA has been suspended.

Twenty-three 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.

<sup>(2)</sup> In alphabetical order: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Finland, Germany, Greece, Latvia, Lithuania, Luxembourg, Romania, Slovakia, Slovenia and Spain.

<sup>(3)</sup> 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.

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

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 CUMYL-4CN-BINACA 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<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:

- 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;
- 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 CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA.

The EMCDDA would like to thank the United States Drug Enforcement Administration for kindly providing unpublished *in vitro* data on the pharmacology of CUMYL-4CN-BINACA (US DEA, 2017).

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.

## 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

1-(4-cyanobutyl)-*N*-(2-phenylpropan-2-yl)indazole-3-carboxamide is commonly referred to as CUMYL-4CN-BINACA.

CUMYL-4CN-BINACA is a synthetic cannabinoid receptor agonist.

CUMYL-4CN-BINACA has an indazole core, which is a common structural feature in many of the synthetic cannabinoids monitored by the EMCDDA. The common name for the substance is derived after its structural features<sup>(6)</sup>: a cumyl group (CUMYL), a cyano group linked to the 4-position (4-CN) of a butyl tail (B), an indazole core (INA), and a carboxamide linker (CA).

Two synthetic cannabinoid receptor agonists have been recently controlled under Schedule II of the United Nations Convention on Psychotropic Substances of 1971: JWH-018<sup>(7)</sup> and AM-2201<sup>(8)</sup>. In addition, MDMB-CHMICA, 5F-APINACA (5F-AKB48) and XLR-11 will be included in the same schedule.

The molecular structure, molecular formula, and molecular mass of CUMYL-4CN-BINACA are provided in Figure 1.

<sup>(4)</sup> 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.

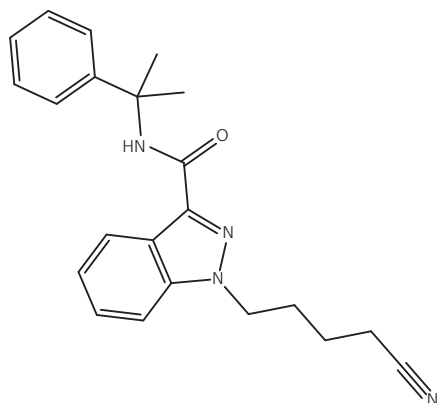
<sup>(5)</sup> A reply was not received from Slovakia.

<sup>(6)</sup> Different naming systems exist and are utilized for applying short/code names to synthetic cannabinoids.

<sup>(7)</sup> Naphthalen-1-yl(1-pentyl-1*H*-indol-3-yl)methanone

<sup>(8)</sup> 1-(5-Fluoropentyl)-1*H*-indol-3-yl]-(naphthalen-1-yl)methanone

FIGURE 1

**Molecular structure, molecular formula, and molecular mass of CUMYL-4CN-BINACA**

	CUMYL-4CN-BINACA
Molecular formula	C <sub>22</sub> H <sub>24</sub> N <sub>4</sub> O
Molecular mass	360.46

CUMYL-4CN-BINACA has a positional isomer, where the cyanobutyl tail is attached to the nitrogen at position 2 of the indazole<sup>(9)</sup>. Both isomers have the same molecular formula and molecular weight which result in very similar mass spectra. However, they can be differentiated based on their retention time and it would be expected that the infrared (IR) and nuclear magnetic resonance spectra (NMR) would be different.

*Commonly used names:*

CUMYL-4CN-BINACA

*Systematic (IUPAC) name:*

1-(4-cyanobutyl)-N-(2-phenylpropan-2-yl)indazole-3-carboxamide

*Other chemical names:*

1-(4-cyanobutyl)-N-(1-methyl-1-phenyl-ethyl)indazole-3-carboxamide;  
 1-(4-cyanobutyl)-N-(1-methyl-1-phenylethyl)-1H-indazole-3-carboxamide;  
 1-(4-cyanobutyl)-N-(2-fenylpropan-2-yl)-1H-indazol-3-karboxamid (Swedish)

*Other names and code names:*

SGT-78; 4-CN-CUMYL-BINACA; CUMYL-CB-PINACA; CUMYL-CYBINACA; 4-cyano CUMYL-BUTINACA

Chemical Abstracts Service (CAS) registry numbers<sup>(10)</sup>:  
 1631074-54-8

IUPAC International Chemical Identifier Key (InChI Key)<sup>(11)</sup>:  
 JGTSOWOPISVAHG-UHFFFAOYSA-N

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.

**Physical description**

In its pure form CUMYL-4CN-BINACA is a crystalline solid.

CUMYL-4CN-BINACA has been seized as a powder and in herbal material. 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**

CUMYL-4CN-BINACA is reported to be stable if stored in accordance with information listed in the safety data sheet<sup>(12)</sup>.

**Detection and analysis**

Reference materials are available for CUMYL-4CN-BINACA<sup>(13)</sup> and CUMYL-4CN-BINACA 2-isomer<sup>(14)</sup>.

Methods documented in the literature for the detection of CUMYL-4CN-BINACA 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, ion chromatography (IC), 1H-NMR and 13C-NMR (Slovenian National Forensic Laboratory, 2016a and 2016b; Bowden and Williamson, 2014).

Quantification of CUMYL-4CN-BINACA in products can be carried out according to the general procedure described by the UNODC (UNODC, 2013).

<sup>(10)</sup> 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.

<sup>(11)</sup> InChI Key is a unique, non-proprietary structural identifier of chemical substances useful in electronic sources.

<sup>(12)</sup> Cayman Chemical, 2016. Safety data sheet of 4-cyano CUMYL-BUTINACA. Available at: <https://www.caymanchem.com/msdss/20194m.pdf>

<sup>(13)</sup> Cayman Chemical Company. '4-cyano CUMYL-BUTINACA', <https://www.caymanchem.com/product/20194>

<sup>(14)</sup> Cayman Chemical Company. '4-cyano CUMYL-BUTINACA isomer 2', <https://www.caymanchem.com/product/20748>

<sup>(9)</sup> The positional isomer of CUMYL-4CN-BINACA is referred to as '4-cyano CUMYL-BUTINACA isomer 2' by Cayman Chemical (<https://www.caymanchem.com/product/20748>).

### 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 16 Member States (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Finland, Germany, Greece, Latvia, Lithuania, Luxembourg, Romania, Slovakia, Slovenia and Spain).

Thirteen countries reported that they have no available information on CUMYL-4CN-BINACA (Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Finland, Greece, Latvia, Lithuania, Luxembourg, Slovakia and Spain).

Three countries provided information on CUMYL-4CN-BINACA (Germany, Romania and Slovenia).

#### The level of production

No information was received in relation to the production of CUMYL-4CN-BINACA.

#### The level of distribution

A total of 20 seizures were reported by two Member States: Germany (19) and Romania (1). Slovenia reported a collected sample (section 3.2.2).

- Germany reported 7 seizures in 2016 (6 small seizures of herbal material and 10 ml of liquid), and 12 seizures in 2017 (10 small seizures of herbal material, and two seizures of 500 and 193 g of powder).
- Romania reported 1 seizure of 0.6 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, 10 Member States (Estonia, France, Germany, Hungary, Lithuania,

Romania, Slovenia, Spain, Sweden and the United Kingdom) and Turkey reported detections of CUMYL-4CN-BINACA (15).

It is important to note that detections of CUMYL-4CN-BINACA may be under-reported since the substance is not routinely screened for. Three Member States (Austria, Slovenia and Sweden) reported that CUMYL-4CN-BINACA is part of routine screening in some (but not all) of their laboratories.

#### Seizures

In total, 2 460 seizures of CUMYL-4CN-BINACA were reported to the EMCDDA by nine Member States and Turkey: Estonia (1 seizure), France (1), Germany (4), Hungary (197), Lithuania (1), Romania (1), Spain (1), Sweden (66), the United Kingdom (2) and Turkey (2 186). The majority of the seizures comprise police and customs cases, with additional seizures taking place in custodial settings.

These seizures included:

- 233 seizures of herbal material, reported by five Member States (Germany, Hungary, Romania, Sweden, the United Kingdom), amounting to a total of 3.6 kg. In addition, Turkey reported 2 186 seizures of herbal material amounting to over 257 kg (16). In the herbal materials seized, CUMYL-4CN-BINACA was commonly found mixed with other synthetic cannabinoids. Seizures included herbal materials, powders, liquids, blotters and unspecified physical forms. A summary is provided below.
- 40 seizures of powder, reported by five Member States (France, Germany, Lithuania, Spain and Sweden), amounting to a total of just under 52 kg. The largest single seizure of powder was reported by Spanish customs, and amounted to 50 kg, which originated in China. In a seizure that took place in January 2017 at Rossy Airport in France, customs intercepted over 1.5 kilograms of powder which also contained the synthetic cathinone 4-CEC (4-chloroethcathinone), on its way from China to the Netherlands.

No quantitative information on purity was provided to the EMCDDA.

#### Collected samples

One collected sample was reported by Slovenia, which consisted of 5 g of off-white powder purchased online from China.

(15) '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.).

(16) This is a minimum estimate provided by the Turkish national focal point.

### Biological samples

Serious adverse events with confirmed exposure to CUMYL-4CN-BINACA from biological samples are discussed in section 3.4.2.

In addition to these, 135 detections where CUMYL-4CN-BINACA was analytically confirmed in biological samples were reported by two Member States: Hungary (133) and Sweden (2) <sup>(17)</sup>. Detections include:

- 16 cases of persons suspected of driving under the influence of drugs (including five traffic accidents), all reported by Hungary;
- 119 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 CUMYL-4CN-BINACA was provided.

#### Money laundering aspects

No information was received on money laundering in connection with the production and/or trafficking of CUMYL-4CN-BINACA.

#### 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 CUMYL-4CN-BINACA.

### 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 CUMYL-4CN-BINACA is a CB<sub>1</sub> receptor agonist (US DEA, 2017) that shares some similarities

with the major psychoactive constituent of cannabis (–)-*trans*-Δ<sup>9</sup>-tetrahydrocannabinol (THC) and synthetic cannabinoids such as JWH-018 and MDMB-CHMICA (EMCDDA, 2017; Järbe and Raghav, 2017; Pertwee, 2014; Reggio, 2009).

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, and, nausea and vomiting. THC also has an abuse liability and dependence potential (Pertwee, 2014; Wiley et al., 2016). Similar effects to THC/cannabis have been reported for synthetic cannabinoids such as CUMYL-4CN-BINACA. In some cases, the effects are reported to be more pronounced/severe (EMCDDA, 2017).

Compared to cannabis, severe and fatal poisoning appears to be more common with synthetic cannabinoids (EMCDDA, 2017; 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.,

<sup>(17)</sup> In addition, Turkey reported 694 samples (blood, hair and urine) which may contain duplicates and therefore have not been included in the total count.

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 CUMYL-4CN-BINACA, 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 reported to the EMCDDA

A total of five acute intoxications with confirmed exposure to CUMYL-4CN-BINACA were reported by Hungary (4 cases) and Sweden (1). The cases occurred during 2016. No further details are available on the cases from Hungary.

In the case from Sweden, it was reported that the individual was found outside and lost consciousness. The patient was treated in intensive care. The only other substances detected were amlodipine and naproxen. No further details are available.

#### Deaths reported to the EMCDDA

A total of 11 deaths with confirmed exposure to CUMYL-4CN-BINACA were reported by Hungary (3 cases) and Sweden (8). The cases in Hungary occurred in 2016. No further details are available on these cases. The cases in Sweden occurred between September 2016 and November 2016.

Of the eight deaths reported by Sweden, seven were male (88 %) and one was female (12 %). The males were aged between 29 and 61 years (mean 43.3, median 40); the female was aged 29. In two cases, no other substances were detected. In the remaining six cases, other substances were detected including central nervous system depressants (such as benzodiazepines, gabapentinoids, and opioids). Where known, most of the individuals were found dead; in at least some cases this was in a home environment. In at least five cases, CUMYL-4CN-BINACA was the cause of death or contributed to the death.

### 3.4.3 Characteristics of users

Similar to other synthetic cannabinoids, CUMYL-4CN-BINACA is sold and used as a 'legal' substitute for cannabis (EMCDDA, 2009; EMCDDA, 2017). It is commonly administered 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 CUMYL-4CN-BINACA.

People who use CUMYL-4CN-BINACA may include recreational users, high-risk drug users, and groups who

experiment with the substance (such as psychonauts). This may also include 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 CUMYL-4CN-BINACA. 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 CUMYL-4CN-BINACA, 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 informed the EMCDDA that CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA dates from 4 March 2016 from the Hungarian national focal point. The Reporting Form details the identification of CUMYL-4CN-BINACA in a seizure of 1 g of green herbal material seized by the Hungarian Police in Orosháza, in January 2016. The substance was analytically confirmed by ATR-FT-IR, GC-MS, <sup>1</sup>H-NMR and <sup>13</sup>C-NMR by the Hungarian Institute for Forensic Science.

CUMYL-4CN-BINACA 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.

It is important to note that CUMYL-4CN-BINACA was first identified in a seizure in Estonia in October 2015. CUMYL-4CN-BINACA was identified in 7.65 g of powder by Customs in Tallinn. The origin of the seizure was the Czech Republic.

### 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)

Seven Member States (Croatia, Cyprus, Finland, Latvia, Lithuania, Luxembourg and Sweden) reported that CUMYL-4CN-BINACA is controlled under drug control legislation.

Four Member States (Austria, Germany, Hungary and Poland) and Turkey reported that CUMYL-4CN-BINACA is controlled under specific new psychoactive substances control legislation.

Sixteen Member States (Belgium, Bulgaria, Czech Republic, Denmark, Estonia, France, Greece, Ireland, Italy, Malta, the Netherlands, Portugal, Romania, Slovenia, Spain and the United Kingdom) reported that CUMYL-4CN-BINACA is not subject to control measures at the national level.

Norway reported that it is not known whether CUMYL-4CN-BINACA is controlled, as the substance is not covered by any

of the generic groups defined in the drug control legislation. It may be covered by the medicinal products legislation if its effects are proved by scientific evidence.

Slovakia did not provide information on the control status of CUMYL-4CN-BINACA.

### 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 CUMYL-4CN-BINACA which has been detected within Europe.

The synthesis of CUMYL-4CN-BINACA was first described in a 2014 patent (Bowden and Williamson, 2014). The patent investigated new indole and indazole cannabinoids and the applications of these compounds.

The published synthetic method for CUMYL-4CN-BINACA (compound 'SGT-78' in the patent) describes the reaction of 1*H*-indazole-3-carboxylic acid (<sup>18</sup>) with 5-bromo-pentanitrile (<sup>19</sup>) to yield 1-(4-cyanobutyl)-1*H*-indazole-3-carboxylic acid (<sup>20</sup>). This substance is then reacted with  $\alpha,\alpha$ -dimethyl-benzenemethanamine (<sup>21</sup>) to give the final product.

#### 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 CUMYL-4CN-BINACA. 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 CUMYL-4CN-BINACA had any

<sup>(18)</sup> CAS number: 4498-67-3

<sup>(19)</sup> aka bromo-4-cyanobutane/4-cyanobutyl-bromide; CAS number: 5414-21-1

<sup>(20)</sup> CAS number: 1185897-54-4

<sup>(21)</sup> Also called 2-phenyl-2-propanamine/cumylamine.

other use apart from in analytical reference materials and scientific research.

From the available information, it does not appear that CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA is used to manufacture a medicinal product for human use.

In addition, the EMA reported that it is not known if CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA is used to manufacture a medicinal product for veterinary use.

In addition, the EMA reported that it is not known if CUMYL-4CN-BINACA is used in the manufacture of medicinal products for veterinary use and which are centrally authorised within the European Union.

#### 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:

- CUMYL-4CN-BINACA has not been granted a marketing authorisation as a medicinal product for human use;
- CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA 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:

- CUMYL-4CN-BINACA has not been granted a marketing authorisation as a medicinal product for veterinary use;
- CUMYL-4CN-BINACA 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 CUMYL-4CN-BINACA as a veterinary medicine.

The EMA also reported that CUMYL-4CN-BINACA:

- 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

CUMYL-4CN-BINACA is a synthetic cannabinoid and a CB<sub>1</sub> receptor agonist. It shares some pharmacological similarities with Δ<sup>9</sup>-tetrahydrocannabinol (THC), which is responsible for the major psychoactive effects of cannabis. In humans, CUMYL-4CN-BINACA appears to cause effects that resemble those of cannabis and other synthetic cannabinoids.

CUMYL-4CN-BINACA has been available in the European Union since at least October 2015 and has been detected in nine Member States and Turkey. More than 270 seizures have been made within the European Union, which includes more than 50 kg of powder and 3.6 kg of herbal material which has been laced with CUMYL-4CN-BINACA. 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 AB-CHMINACA available on the market was synthesised by chemical companies based in China.

Eleven deaths with confirmed exposure to CUMYL-4CN-BINACA have been reported by two Member States. In at least five of the deaths, CUMYL-4CN-BINACA was the cause of death or contributed to the death.

CUMYL-4CN-BINACA is currently not under assessment and has not been under assessment by the UN system. CUMYL-4CN-BINACA is not subject to control measures in 16 Member States.

We conclude that the health and social risks caused by the manufacture, trafficking and use of CUMYL-4CN-BINACA, 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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## Annex 1

Images from seizures and collected samples provided to the EMCDDA

Country	Image	
Slovenia	 <p data-bbox="507 869 807 936"><b>CUMYL-4CN-BINACA</b> <b>KEM ID: 1666-16</b></p>	<p data-bbox="1107 371 1490 450">Collected sample, 4 October 2016 White powder Collecting authority: project RESPONSE</p>

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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.

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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.

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