World Health Organization

# Critical review report:

# Dipentylone

**Expert Committee on Drug Dependence**

**Forty-sixth Meeting**

**Geneva, 16-20 October 2023**

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## Executive summary

Dipentylone (IUPAC name: 1-(1,3-benzodioxol-5-yl)-2-(dimethylamino)pentan-1-one, also known as *N*,*N*-dimethylpentylone, dimethylpentylone or bk-DMBDP) is a synthetic cathinone with a chemical structure and pharmacological similar to those of other Schedule I (under the 1961 United Nations Conventions) synthetic cathinones (e.g. methylone) and other Schedule I and II (under the 1961 United Nations Conventions) psychostimulants (e.g. cocaine, methamphetamine, 3,4-methylenedioxymethamphetamine [MDMA]). No medical use of dipentylone was identified. Dipentylone has not previously been reviewed by the WHO Expert Committee on Drug Dependence.

Reports from law enforcement encounters and from people who use dipentylone indicate that dipentylone is mainly taken orally and can be also smoked. It is commonly sold as other substances (e.g. MDMA, 2C-B, alprazolam, 4-MMC).

No reports were found on the absorption, distribution, metabolism or excretion of dipentylone. Nevertheless, pentylone has often been detected with dipentylone, but at a lower concentration, suggesting that pentylone is a metabolite of dipentylone.

The binding affinity of dipentylone to the dopamine transporter (DAT) is more similar to that of cocaine than to that of methamphetamine or MDMA. Dipentylone was about twice as potent in inhibiting dopamine uptake as cocaine or MDMA but less potent than METH. Dipentylone stimulated locomotor activity in mice in a time- and dose-dependent manner.

Dipentylone has been identified in several toxicology cases, including antemortem and postmortem investigations; however, the toxic doses of dipentylone were not provided. Reported adverse effects included increased energy, enhanced senses, relaxation, increased confidence, euphoria, empathy, insomnia, memory loss, paranoia and confusion.

No studies of its dependence potential in animals or humans were identified. In drug discrimination studies in rats, dipentylone fully substituted for the discriminative stimulus effects of cocaine and methamphetamine, suggesting its potential for abuse. It substituted only partially for the discriminative stimulus effects of MDMA. No studies of the abuse potential of dipentylone in experimental animals or humans were identified, but its structural similarities with other synthetic cathinones and controlled substances suggest that it has potential for abuse by humans.
Dipentylone has no known therapeutic or industrial uses or any marketing authorizations.

Dipentylone was first detected in Sweden and in Kansas (USA) in 2014. Since then, dipentylone has been detected in 33 US states. Dipentylone is not currently controlled under the 1961, 1971 or 1988 United Nations Conventions but is controlled under legislation in a number of countries.

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# 1 Substance identification

### *A International Nonproprietary Name*

Not assigned

### *B Chemical Abstracts Service (CAS) Registry Number*

803614-36-0 (free base)
17763-13-2 (hydrochloride salt)
2304915-61-3 ((*S*)-enantiomer)
2304915-25-9 ((*R*)-enantiomer)

### *C Other chemical names*

1-(1,3-Benzodioxol-5-yl)-2-(dimethylamino)-1-pentanone (ACI)
Valerophenone, 2-(dimethylamino)-3',4'-(methylenedioxy)- (8CI)
Dipentylone
*N*,*N*-Dimethylpentylone

### *D Trade names*

Dipentylone hydrochloride is sold under the name *N*,*N*-dimethylpentylone (hydrochloride) as an analytical reference standard *(1)*.

### *E Street names*

The chemical names listed above may be used as street names. Other names include DMBDP, Bk-dmbdp, betaK-Dmbdp BU crystal).

### *F Physical appearance*

Dipentylone hydrochloride is described as a neat solid; for recreational use, dipentylone is distributed mainly as crystals or tablets *(2)*.

### *G WHO review history*

Dipentylone has not been formally reviewed by WHO and is not currently under international control.

## 2 Chemistry

### *A Chemical name*

**IUPAC Name:** 1-(1,3-Benzodioxol-5-yl)-2-(dimethylamino)pentan-1-one

**CA Index Name:** 1-Pentanone, 1-(1,3-benzodioxol-5-yl)-2-(dimethylamino)- (ACI)

**Free base:**

Canonical SMILES

O=C(C1=CC=C2OCOC2=C1)C(N(C)C)CCC

InChI

InChI=1S/C14H19NO3/c1-4-5-11(15(2)3)14(16)10-6-7-12-13(8-10)18-9-17-12/h6-8,11H,4-5,9H2,1-3H3

InChI Key

PQTJKFUXRBKONZ-UHFFFAOYSA-N

***Hydrochloride salt***

Canonical SMILES

Cl.O=C(C1=CC=C2OCOC2=C1)C(N(C)C)CCC

InChI

InChI=1S/C14H19NO3.ClH/c1-4-5-11(15(2)3)14(16)10-6-7-12-13(8-10)18-9-17-12;/h6-8,11H,4-5,9H2,1-3H3;1H

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InChI Key

LSDMAZIZKMMYTB-UHFFFAOYSA-N

***(2R)-enantiomer***

Canonical SMILES

O=C(C1=CC=C2OCOC2=C1)C(N(C)C)CCC

Isomeric SMILES

C([C@@H](CCC)N(C)C)(=O)C=1C=C2C(=CC1)OCO2

InChI

InChI=1S/C14H19NO3/c1-4-5-11(15(2)3)14(16)10-6-7-12-13(8-10)18-9-17-12/h6-8,11H,4-5,9H2,1-3H3/t11-/m1/s1

InChI Key

PQTJKFUXRBKONZ-LLVKDONJSA-N

***(2S)-enantiomer***

Canonical SMILES

O=C(C1=CC=C2OCOC2=C1)C(N(C)C)CCC

Isomeric SMILES

C([C@H](CCC)N(C)C)(=O)C=1C=C2C(=CC1)OCO2

InChI

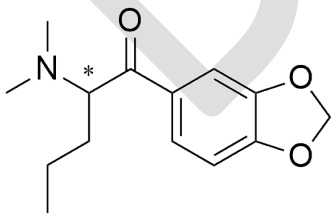
InChI=1S/C14H19NO3/c1-4-5-11(15(2)3)14(16)10-6-7-12-13(8-10)18-9-17-12/h6-8,11H,4-5,9H2,1-3H3/t11-/m0/s1

InChI Key

PQTJKFUXRBKONZ-NSHDSACASA-N

## *B Chemical structure*

***Free base:***




**Molecular formula:** $C_{14}H_{19}NO_3$

**Molecular weight:** 249.31 g/mol

## *C Stereoisomers*

Dipentylone contains a chiral centre. Thus, two enantiomers may exist: (R)-dipentylone and (S)-dipentylone. No information was available on the enantiomeric composition of dipentylone circulating on the drug market, but it is most likely to be available as a racemic



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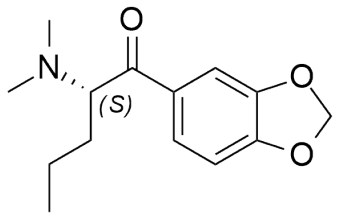
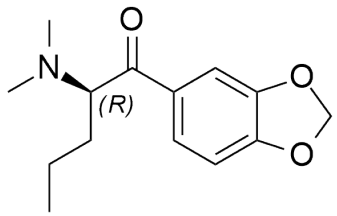
mixture of the (R)- and (S)- enantiomers; the occurrence of individual stereoisomers cannot be excluded.




(2S)-1-(1,3-Benzodioxol-5-yl)-2-(dimethylamino)pentan-1-one

CAS RN 2304915-61-3




(2R)-1-(1,3-Benzodioxol-5-yl)-2-(dimethylamino)pentan-1-one

CAS RN 2304915-25-9

## *D Methods and ease of illicit manufacture*

No specific information was available on the routes of synthesis used for the dipentylone products circulating on the market. The first synthesis of dipentylone was described in 1967 in a patent *(3)*. The chemical synthesis of cathinones is facile and usually involves two steps. An α-bromoketone ([1-(1,3-benzodioxol-5-yl)-2-bromo-1-pentanone] is obtained from the appropriate arylketone [1-(benzo[*d*][1,3]dioxol-5-yl]pentan-1-one, followed by nucleophilic substitution with an appropriate amine (dimethylamine) to give the corresponding cathinone (dipentylone). Cathinones are generally isolated as their salts because of the instability of the free base *(4)*. This procedure has also been used for the preparation of dipentylone analogues. The ketone species 1-(1,3-benzodioxol-5-yl)-2-bromo-1-pentanone (**2**) is accessible by various routes and is commercially available.

While the total synthesis of dipentylone requires qualified personnel and a well-equipped synthetic laboratory, preparation by amination of **2** is easier, requires simpler equipment and can be performed by unqualified personnel.

## *E Chemical properties*

*Melting-point*

Dipentylone hydrochloride, 225–228 °C *(3)*

*Boiling-point*

No information was found.

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*Solubility*

Dipentylone hydrochloride: 5 mg/mL in methanol, 1 mg/mL in phosphate-buffered saline (pH 7.2) *(1)*

### *F Identification and analysis*

Dipentylone hydrochloride salt and the deuterated species dipentylone-$d_6$ hydrochloride salt are available as reference materials from commercial suppliers for use in routine analysis in forensic and clinical investigations *(1)*.

Dipentylone in seized material can be identified and quantified according to the general procedure described for cathinones by the United Nations Office on Drugs and Crime, with presumptive colour tests and confirmation by gas chromatography (GC)–mass spectrometry (MS) and GC–Fourier transform-infrared (FT-IR) spectroscopy *(4)*.

Pure dipentylone hydrochloride has been fully characterized by proton and carbon nuclear magnetic resonance, FT-IR spectroscopy and GC-MS *(5,6)*.

Dipentylone was detected in some wastewaters samples and was quantified by ultra-high-performance liquid chromatography (LC) and µLC coupled to MS:MS in Italy in 2019 *(7)* and by LC-MS:MS in Spain in 2018 *(8)*.

The enantiomers of dipentylone (purchased online) were separated by chiral LC-ultraviolet *(9)*.

Analytical methods were developed for determination of dipentylone in urine samples by either LC-triple quadropole LC:MS:MS *(10)* or LC-high-resolution MS *(11)*. Dipentylone was determined in oral fluid by LC-MS:MS with a limit of detection of 0.1 ng/mL *(12)*. In the same work, stability studies showed that dipentylone is stable at ambient temperature for 15 days, at 4 °C for 60 days and at –20 °C for 90 days *(12)*.

## 3 Ease of conversion into controlled substances

No information was available on whether dipentylone can be converted into a controlled substance or how easy it would be.

## 4 General pharmacology

### *A Routes of administration and dosage*

Unverified media reports described people buying dipentylone in “chunks” and then cutting them into powder to snort, inject or smoke *(13).*

Posts on online forums (e.g. BlueLight) and reports to the Welsh Emerging Drugs and Identification of Novel Substances Project indicate that dipentylone may be smoked *(14)* or taken orally *(15)*.

No reports on dosage were found.

### *B Pharmacokinetics*

No data on the absorption, distribution, metabolism, and excretion of dipentylone were found.

Pentylone is suspected to be a metabolite of dipentylone, as it was detected in the blood of a series of 18 post-mortem cases in which dipentylone was identified, but at a lower concentration than dipentylone *(16)*. Similarly, data from the Center for Forensic Science Research and Education (CFSRE) indicated the presence of pentylone at lower concentrations (120 ± 170 ng/mL, range: 10–420 ng/mL) than dipentylone (270 ± 400 ng/mL, range: 33–970 ng/mL) in a series of 32 toxicological cases, further indicating pentylone is a metabolite of dipentylone *(17)*. Co-ingestion of pentylone and dipentylone cannot, however, be ruled out. Laboratories should always ascertain the presence of dipentylone when pentylone is detected.

### *C Pharmacodynamics*

The interaction of dipentylone with monoamine transporters was determined by testing the effects of dipentylone on radioligand ([$^{125}$I]RTI-55) binding and [$^{3}$H]neurotransmitter (i.e. dopamine, serotonin, norepinephrine) uptake by HEK cells expressing cDNA for the human dopamine transporter (HEK-hDAT cells), the human serotonin transporter (HEK-hSERT cells) and the human norepinephrine transporter (HEK-hNET cells). Dipentylone showed higher affinity for DAT (Ki = 0.354 ± 0.073 µM) than NET (Ki = 2.00 ± 0.34 µM) or SERT (Ki = 2.27 ± 0.30 µM), as it was equipotent in inhibiting NET ($IC_{50}$ = 0.212 ± 0.068 µM) and DAT ($IC_{50}$ = 0.233 ± 0.066 µM), and was about 10 times more selective in inhibiting DAT and NET than SERT ($IC_{50}$ = 2.57 ± 0.55 µM) (Table 1). As also shown in Table 1, the affinity of dipentylone to DAT was more similar to that of cocaine than to that of methamphetamine or MDMA (about 12 and 88 times higher, respectively). Dipentylone was about two times more potent in inhibiting dopamine uptake than cocaine or MDMA but less potent (about 2.4 times) than methamphetamine. It also showed much higher affinity to SERT than methamphetamine or MDMA (about 66 and 8 times higher, respectively) but lower (about 4.5 times) affinity than cocaine and higher potency (about 3.6 times) than methamphetamine and lower activity than cocaine and MDMA (about 7 and 22 times, respectively) in inhibiting serotonin uptake. Dipentylone showed similar binding affinity to NET as cocaine and methamphetamine but lower than that of MDMA (about 8 times) and about 2 and 3 times higher potency in inhibiting norepinephrine uptake than cocaine and MDMA, respectively, but was about 10 times less potent than methamphetamine in inhibiting the uptake of this neurotransmitter.

**Table 1. Effects of dipentylone, cocaine, methamphetamine and MDMA on [$^{125}$I]RTI-55 binding and [$^{3}$H]neurotransmitter uptake by HEK-hDAT, HEK-hSERT and HEK-hNET cells (mean ± SEM)**

| HEK-hDAT | Dipentylone | Cocaine | Methamphetamine | MDMA |
|---|---|---|---|---|
| [$^{125}$I]RTI-55 binding: Ki ± SEM (µM) (*n*) | 0.354 ± 0.073 (3) | 0.495 ± 0.049 (22) | 4.41 ± 0.43 (20) | 31.0 ± 4.9 (6) |
| [$^{3}$H)DA uptake: IC50 ± SEM (µM) *(n)* | 0.233 ± 0.066 (3) | 0.425 ± 0.036 (23) | 0.097 ± 0.013 (21) | 0.479 ± 0.070 (4) |
| HEK-hSERT | | | | |
| [$^{125}$I]RTI-55 binding: Ki ± SEM (µM) (*n*) | 2.27 ± 0.30 (3) | 0.495 ± 0.034 (20) | 150 ± 17 (20) | 17.5 ± 3.3 (6) |

| | | | | |
|---|---|---|---|---|
| [$^3$H]5-HT uptake :IC50 ± SEM (µM) (*n*) | 2.57 ± 0.55 (5) | 0.364 ± 0.040 (24) | 9.3 ± 1.1 (18) | 0.118 ± 0.019 (4) |
| HEK-hNET | | | | |
| [$^{125}$I]RTI-55 binding: Ki ± SEM (µM) (*n*) | 2.00 ± 0.34 (3) | 1.95 ± 0.15 (18) | 2.51 ± 0.24 (16) | 15.8 ± 4.1 (7) |
| [$^3$H]NE uptake:IC50 ± SEM (µM) (*n*) | 0.212 ± 0.068 (4) | 0.382 ± 0.037 (23) | 0.0258 ± 0.0030 (19) | 0.63 ± 0.14 (3) |

Adapted from Eshleman et al. *(18)*

Dipentylone (administered at 2.5, 5, 10, 25 or 50 mg/kg immediately before testing for locomotor activity) stimulated locomotor activity time- and dose-dependently, assessed by measuring horizontal activity, i.e. interruption of horizontal photocell beams on the sides of each activity chamber, for 8 h, within 10-min periods, in a group of male Swiss-Webster mice. Increased locomotor activity was observed after 10 and 25 mg/kg, with peak effects after administration of 25 mg/kg, which occurred within 10 min and lasted 360 min. A dose of 50 mg/kg returned locomotor activity to baseline levels. The locomotor activity potency of dipentylone was similar to that of cocaine ($ED_{50}$ = 5.29 ± 0.09 mg/kg vs 5.03 ± 0.06 mg/kg, for dipentylone and cocaine, respectively) but lower than that of methamphetamine ($ED_{50}$ = 0.41 ± 0.05 mg/kg) *(19)*.

Similar results were obtained by Sumien et al. *(20)*, who found that intraperitoneal injection of male Swiss-Webster mice with 1, 2.5, 5, 10, 25 or 50 mg/kg dipentylone immediately before locomotor activity testing stimulated horizontal activity in a time- and dose-dependent manner at 5–50 mg/kg. Doses of 5–25 mg/kg stimulated activity within 10 min of injection and lasted 80–220 min. For the 30-min period in which maximal stimulant effects occurred, the $ED_{50}$ was estimated to be 6.4 mg/kg; the peak effect was estimated to be 6539 counts/10 min at 14.2 mg/kg. The maximum locomotor activity in mice administered cocaine was estimated to be 5593 counts/10 min at 12.7 mg/kg, with an estimated potency ($ED_{50}$) of 2.5 mg/kg. For mice injected with METH, the maximum locomotor activity was estimated at 6653 counts/10 min at 1.2 mg/kg, with an $ED_{50}$ of 0.51 mg/kg.

# 5 Toxicology

Dipentylone was first identified in toxicological samples in the USA in the third quarter of 2021. By April 2022, dipentylone had been identified in 32 toxicology cases, including ante- and post-mortem investigations, in addition to cases of drug material *(17)*.

Recently, dipentylone was detected in 18 post-mortem cases at concentrations of 3.3–970 ng/mL (median: 145 ng/mL, mean 277 ± 283 ng/mL). In all cases, dipentylone was found in combination with other substances, namely fentanyl (n=7), eutylone (n=6) and methamphetamine/amphetamine (n=5). Sixty-two additional cases were pending analysis *(16)*.

Dipentylone was found in a post-mortem sample (by GC-MS/MS) in New Zealand in 2021 *(21)*. Also in New Zealand, “serious harm” was linked to consumption of dipentylone, in combination with bromazolam misrepresented as MDMA *(22)*.

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Two fatal cases involving dipentylone were reported by the US Drug Enforcement Agency in 2023. Dipentylone was detected at a concentration of 83.4 ng/mL in a 58-year-old male in Tennessee who had a medical history of intravenous use of drugs, including cocaine. Methamphetamine (2500 ng/mL), fentanyl (36.6 ng/mL) and pentylone (10.7 ng/mL) were also detected. Dipentylone (0.3 ng/mL) was also found in a 34-year-old male in Tennessee with a history of tobacco and alcohol use and previous reports in the Controlled Substances Monitoring Database of hydrocodone (October 2022) and oxycodone (November 2022).

No reports were found on the toxic doses of dipentylone for humans.

# 6 Adverse reactions in humans

A media report described the effects of dipentylone as similar to those of other narcotic stimulants *(13)*.

An individual who brought a sample to KnowYourStuffNZ for checking reported that they had taken the substance and described the experience as "very unenjoyable". They had also experienced a bad "comedown", during which they felt anxious *(23)*.

A post on the Bluelight forum reported that smoking dipentylone was "very bad for the lungs" and produced a bad taste (described as "resembling diesel fuel") and "nasty burning" *(14)*.

Reports to the Welsh Emerging Drugs and Identification of Novel Substances Project indicated the following adverse reactions after oral intake of dipentylone: increased energy (5), enhanced senses (4), relaxation (5), increased confidence (5), euphoria (3), empathy (3), insomnia (3), memory loss (3), paranoia (2), confusion (2), hallucinations (1), panic attack (1), agitation (1), breathlessness (1), irregular heartbeat (1), depression (1) and suicidal ideation (1) *(15)*.

# 7 Dependence potential

## *A Studies in experimental animals*

No studies were identified.

## *B Studies in humans*

No studies were identified.

# 8 Abuse potential

## *A Studies in experimental animals*

Dipentylone (at 2.5, 5, 10 and 25 mg/kg) was tested for substitution in a two-lever choice method with Sprague-Dawley rats trained to discriminate methamphetamine (1 mg/kg), cocaine (10 mg/kg) or MDMA (1.5 mg/kg) from saline *(19)*. Dipentylone fully substituted for the discriminative stimulus effects of methamphetamine ($ED_{50}$ = 8.70 ± 0.12 mg/kg) and cocaine ($ED_{50}$ = 8.27 ± 0.12 mg/kg), indicating abuse potential *(19,20)*. In the methamphetamine-trained rats, dipentylone increased the response rate after injection of 5 and 10 mg/kg, with the maximum effect (152% of vehicle control) at 10 mg/kg. The effect decreased to 52% of the vehicle control after 25 mg/kg. In the cocaine-treated rats, dipentylone (1–25 mg/kg) did not change the response rate from that of the vehicle control *(19,20)*. Dipentylone only partially substituted for the discriminative stimulus of MDMA,

producing a maximum 60% MDMA-appropriate response after 25 mg/kg. The response rate was increased to 155% of vehicle control after 10 mg/kg and decreased to 18% of vehicle control after 50 mg/kg, such that only two of six rats earned a reinforcer *(19,24)*.

### *B Studies in humans*

No studies on the abuse potential of dipentylone in humans were identified.

One person who reported dipentylone use on an online forum described inability to stop taking it *(14)*.

## 9 Therapeutic applications and extent of therapeutic use and epidemiology of medical use

Dipentylone is not known to have any medical use.

## 10 Listing on the WHO Model List of Essential Medicines

Dipentylone is not listed on the 23rd WHO List of Essential Medicines or the 8th WHO List of Essential Medicines for Children.

## 11 Marketing authorizations (as a medicinal product)

Dipentylone is not known to be authorized for marketing in any country.

## 12 Industrial use

Dipentylone is not known to have any industrial use.

## 13 Non-medical use, abuse and dependence

Dipentylone was detected in wastewater for the first time in 2019 in a study in Spain for determination of the presence of illicit drugs and new psychoactive substances in sewage. It was detected at a concentration of 6.4 ng/L in one of the eight wastewater treatment plants analysed. No further information was provided about the characteristics of the wastewater treatment plants (location, area or population represented) *(7)*. In a study of wastewater samples collected in 13 Spanish cities (covering 6 million inhabitants, corresponding to 12.8% of the Spanish population), the same authors reported the presence of dipentylone in samples of wastewater in Valencia *(8)*.

## 14 Nature and magnitude of public health problems related to misuse, abuse and dependence

No information was found on the nature or magnitude of public health problems associated with the use of dipentylone.

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Dipentylone has, however, been confirmed in biological fluids from post-mortem cases. Furthermore, dipentylone has frequently been detected in products that were mislabelled and/or sold as other substances (e.g. MDMA, 2C-B, alprazolam, 4-MMC or mephedrone), suggesting that most people who use dipentylone are unaware of its identity.

## 15 Licit production, consumption and international trade

Dipentylone is used as reference material in scientific research and forensic applications.

## 16 Illicit manufacture and traffic and related information

Dipentylone was first detected in Sweden in 2014 *(25)*. Reports from the US National Forensic Laboratory Information System (NFLIS-Drug) indicate that dipentylone was first detected in the USA in 2014, in Kansas *(26)*. Since then, dipentylone has been detected in 33 US states, in a total of 6169 reports submitted to NFLIS-Drug. Florida (4662) and Virginia (577) contributed most reports on dipentylone *(26)*.

In 2022, 4901 reports on dipentylone were made to NFLIS-Drug. In the 2880 reports that included weights, the total was 64 586.71 g. Data collected between August 2021 and March 2022 from Arkansas (1), District of Columbia (1), Florida (17), Georgia (1), New Jersey (1), New York (2), Pennsylvania (1), Virginia (5) and West Virginia (2) indicated that dipentylone was found in at least one case of driving under the influence of drugs and at least 26 fatal poisonings or deaths. Five other toxicological cases had unknown outcomes. Aegis Sciences Corporation detected 15 cases in 2021 and 45 cases in the first half of 2022 (January–June). The Center for Forensic Science Research and Education with “NPS Discovery” reported 166 positive cases between the first quarter of 2020 and the first quarter of 2023 *(26)*.

A 45-year-old man in Syracuse (NY, USA) pleaded guilty to distributing controlled substances, including, on 10 March 2022, giving another individual approximately 770 g of dipentylone to deliver to a customer in Oswego (NY, USA). This individual admitted that, on the same date, he possessed approximately 7 kg of dipentylone, which he intended to distribute to others *(27)*.

The US Customs and Border Protection seized 32.2 kg of dipentylone, labelled "beauty products", sent from China to an address in Washington DC in June 2023 *(28)*.

In July 2023, an assistant special agent of the US Drug Enforcement Administration reported that dipentylone was found in the possession of people attending nightclubs and bars in the Jacksonville, Florida (USA) area *(13)*. Dipentylone was reported to cost US$ 150–200 per ounce (23 g).

Dipentylone was first detected in New Zealand in 2017. In 2022 and 2023, a total of 29.9 kg of this substance was detected at 43 border seizures and drug checking of samples (volume and number of detections not quantified). The presence of dipentylone was confirmed in two coronial cases in New Zealand *(21)*. The drug early warning website High Alert in New Zealand issued its first alert about detection of dipentylone. Dipentylone was found in two samples tested by KnowYourStuffNZ in Dunedin, including in a pink “Playboy” tablet that was sold as MDMA *(23)*.

Dipentylone was first detected in Canada in 2022, in 11 cases in Ontario, by the Health Canada Drug Analysis Service *(29)*.

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## 17 Current international controls and their impact

Dipentylone is not currently controlled under the 1961, 1971 or 1988 United Nations Conventions.

## 18 Current and past national controls

In Germany, dipentylone is classified as "Neue-psychoaktive-Stoffe-Gesetz (NpSG)", which authorizes its use only for industrial and scientific purposes.

In New Zealand, dipentylone is regulated as a Class C7 controlled drug under the Misuse of Drugs Act 1975, as an analogue of MDMA.

Dipentylone is controlled as a Class B drug under the United Kingdom Misuse of Drugs Act.

Dipentylone is not explicitly scheduled in the USA; however, it could be considered an isomer of the Schedule I substance *N*-ethyl pentylone.

## 19 Other medical and scientific matters relevant for a recommendation on scheduling of the substance

Dipentylone appears to be commonly sold as cocaine or MDMA in New Zealand and the USA *(17,23)*. Hence individuals who use it may be unaware of its identity. Moreover, in all 16 sample analyses reported by the Welsh Emerging Drugs and Identification of Novel Substances Project in which dipentylone was confirmed, the purchaser had intended to buy another substance, including MDMA (7 cases), 2C-B (6 cases), alprazolam (1 case), 4-MMC (1 case) and mephedrone (1 case).

# References


1. N,N-Dimethylpentylone (hydrochloride) (Item No. 9001933). Ann Arbor (MI): Cayman Chemicals Company; 2021 (https://www.caymanchem.com/product/9001933/n%2Cn-dimethylpentylone-(hydrochloride), accessed 4 July 2023).
2. Cornish S. The new drug arriving at our borders posing a significant risk. Wellington: Stiff; 2022 (https://www.stuff.co.nz/national/128753223/the-new-drug-arriving-at-our-borders-posing-a-significant-risk, accessed 4 July 2023).
3. Koeppe H, Ludwig G, Zeile K. Substituted phenyl-α-amino ketones. German patent no. DE1545591A1 to Boehringer Sohn AG and Co KG; 1967 (https://patents.google.com/patent/DE1545591A1/en).
4. Recommended methods for the identification and analysis of synthetic cathinones in seized materials. Vienna: United Nations Office on Drugs and Crime; 2020 (https://www.unodc.org/unodc/en/scientists/recommended-methods-for-the-identification-and-analysis-of-synthetic-cathinones-in-seized-materials.html).
5. Analytical data for dipentylone. Budapest: Hungarian Institute for Forensic Science; 2016 (https://www.policija.si/apps/nfl_response_web/seznam.php).
6. Sisco E, Burns A, Moorthy AS. Development and evaluation of a synthetic cathinone targeted gas chromatography mass spectrometry (GC-MS) method. J Forensic Sci. 2021;66(5):1919–28. doi:10.1111/1556-4029.14789.
7. Celma A, Sancho JV, Salgueiro-González N, Castiglioni S, Zuccato E, Hernández F et al. Simultaneous determination of new psychoactive substances and illicit drugs in sewage: Potential of micro-liquid chromatography tandem mass spectrometry in wastewater-based epidemiology. J Chromatogr A. 2019;1602:300–9. doi:10.1016/j.chroma.2019.05.051.


DRAFT

8. Bijlsma L, Picó Y, Andreu V, Celma A, Estévez-Danta A, González-Mariño I et al. The embodiment of wastewater data for the estimation of illicit drug consumption in Spain. Sci Total Environ. 2021;772:144794. doi:10.1016/j.scitotenv.2020.144794.
9. Kadkhodaei K, Forcher L, Schmid MG. Separation of enantiomers of new psychoactive substances by high-performance liquid chromatography. J Sep Sci. 2018;41(6):1274–86. doi:10.1002/jssc.201701239.
10. Chen JY, Chen GY, Wang SY, Fang CC, Chen LY, Weng TI. Development of an analytical method to detect simultaneously 219 new psychoactive substances and 65 other substances in urine specimens using LC-QqQ MS/MS with CriticalPairFinder and TransitionFinder. Talanta. 2022;238(1):122979. doi:10.1016/j.talanta.2021.122979.
11. Stephanson NN, Signell P, Helander A, Beck O. Use of LC-HRMS in full scan-XIC mode for multi-analyte urine drug testing – a step towards a "black-box" solution? J Mass Spectrom. 2017;52(8):497–506. doi:10.1002/jms.3946.
12. da Cunha KF, Oliveira KD, Huestis MA, Costa JL. Screening of 104 new psychoactive substances (NPS) and other drugs of abuse in oral fluid by LC-MS-MS. J Anal Toxicol. 2020;44(7):697–707. doi:10.1093/jat/bkaa089.
13. Newest drug to hit the streets makes its way to northeast Florida nightclubs, bars. Jacksonville (FL): News4JAX; 2023 (https://www.news4jax.com/news/local/2023/07/11/newest-drug-to-hits-the-streets-makes-its-way-to-northeast-florida-nightclubs-bars/, accessed 28 July 2023).
14. Bluelight; 2023 (http://www.bluelight.org, accessed 29 July 2023).
15. Sample results for dipentlyone. Cardiff: Welsh Emerging Drugs and Identification of Novel Substances Project; 2023 (https://www.wedinos.org/sample-results#mylocation, accessed 24 July 2023).
16. Fogarty MF, Krotulski AJ, Papsun DM, Walton SE, Lamb M, Truver MT et al. *N*,*N*-Dimethylpentylone (dipentylone) – A new synthetic cathinone identified in a postmortem forensic toxicology case series. J Anal Toxicol. 2023. doi:10.1093/jat/bkad037.
17. Krotulski AJ, Fogarty MF, Papsun DM, Lamb M, Walton SE, Logan BK. Synthetic stimulant market rapidly changing as N,N-dimethylpentylone replaces eutylone in drug supply typically sold as "ecstasy" or "molly". Philadelphia (PA): Center for Forensic Science Research and Education; 2022 (https://www.drugsandalcohol.ie/36120/).
18. Eshleman AJ, Nagarajan S, Wolfrum KM, Reed JF, Swanson TL, Nilsen A et al. Structure–activity relationships of bath salt components: substituted cathinones and benzofurans at biogenic amine transporters. Psychopharmacology. 2019;236(3):939–52. doi:10.1007/s00213-018-5059-5.
19. Gatch MB, Shetty RA, Sumien N, Forster MJ. Behavioral effects of four novel synthetic cathinone analogs in rodents. Addict Biol. 2021;26(4):e12987. doi:10.1111/adb.12987.
20. Sumien N, Shetty RA, Forster MJ. Time-course (8-h) mouse locomotor activity test vs cocaine and (+)-methamphetamine time courses. 2018 Contract Nr. N01DA-13-8908 (HHSN271201300001). Department of Pharmacology & Neuroscience, University of North Texas Health Science Center, Fort Worth, Texas, USA. 2019.
21. Fearn D, Kappatos D, Russell S, Murray A, Johnson C, McCarthy MJ. First confirmation of synthetic cathinone N,N-dimethylpentylone in postmortem sample in New Zealand using GC-MS/MS. Toxicol Anal Clin. 2022;34(3_Suppl):S111–2. doi:10.1016/j.toxac.2022.06.177.
22. Misrepresented MDMA linked to serious harm in Hawke's Bay. Wellington: High Alert; 2023 (https://highalert.org.nz/alerts-and-notifications/misrepresented-mdma-linked-to-serious-harm-in-hawkes-bay/, accessed 21 August 2023).
23. New synthetic cathinone dimethylpentylone detected in NZ. Wellington: High Alert; 2021 (https://highalert.org.nz/alerts-and-notifications/new-synthetic-cathinone-dimethylpentylone-detected-in-nz, accessed 28 July 2023).
24. Gatch MB, Forster MJ. Test of substitution for the discriminative stimulus effects of 3,4-methylenedioxymethamphetamine. Contract Nr. N01DA-18-8936 (HHSN271201800031) 2019.


DRAFT

25. Europol 2014 Annual Report on the implementation of Council Decision 2005/387/JHA. Luxembourg: European Monitoring Centre for Drugs and Drug Addiction; 2014 (https://www.emcdda.europa.eu/publications/implementation-reports/2014_en).
26. DIpentylone summary. Springfield (VA): National Forensic Laboratory Information System; 2023.
27. Syracuse man pleads guilty to distribution of "molly". Arlington (VA): Drug Enforcement Administration; 2022 https://www.dea.gov/press-releases/2022/07/15/syracuse-man-pleads-guilty-distribution-molly, accessed 28 July 2023).
28. Dulles CBP officers seize 70 pounds of a dangerous, newer cathinone analogue destined to D.C. Washington DC: US Customs and Border Protection; 2023 https://www.cbp.gov/newsroom/local-media-release/dulles-cbp-officers-seize-70-pounds-dangerous-newer-cathinone-analogue, accessed 28 July 2023).
29. Canada – dipentylone. Ottawa: Health Canada, Drug Analysis Service; 2023

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