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Subject:	Risk assessment report on a new psychoactive substance: 1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one (**α**-pyrrolidinovalerophenone, **α**-PVP) In accordance with Article 6 of Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances

Following the Council's request to conduct a Risk Assessment on a new psychoactive substance, 1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one (**α**-pyrrolidinovalerophenone, **α**-PVP), the EMCDDA hereby presents the above-mentioned Risk Assessment Report drawn up by its Scientific Committee pursuant to Article 6 of Council Decision 2005/387/JHA on information exchange, risk assessment and control of new psychoactive substances.

European Monitoring Centre
for Drugs and Drug Addiction

Risk assessment report on a new psychoactive substance:
1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one
(α-pyrrolidinovalerophenone, α-PVP)

In accordance with Article 6 of Council Decision 2005/387/JHA on the information exchange, risk assessment and control of new psychoactive substances

Contents

1. Introduction

This risk assessment report presents the summary findings and the conclusion of the risk assessment carried out by the extended Scientific Committee of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) on the new psychoactive substance 1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one, commonly known as **α**-pyrrolidinovalerophenone (**α**-PVP). The report is intended for policy makers and decision makers in the institutions of the European Union.

The report has been prepared and drafted in accordance with the conceptual framework and the procedure set out in the risk assessment operating guidelines ([1]). It is written as a stand-alone document, which presents a summary of the information considered during the detailed analysis of the scientific and law enforcement data available at this time. The conclusion section of the report summarises the main issues addressed and reflects the opinions held by the members of the Scientific Committee. A list of the information resources considered by the Scientific Committee, including a detailed technical report on **α**-PVP, is provided below. This risk assessment report should be read and understood in conjunction with the technical report on **α**-PVP (Annex 1).

The risk assessment has been undertaken in compliance with Article 6 of Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk assessment and control of new psychoactive substances ([2]) (hereafter 'Council Decision'). The Council Decision establishes a mechanism for the rapid exchange of information on new psychoactive substances (hereafter 'EU Early Warning System' ([3])) that may pose public health and social threats, including those related to the involvement of organised crime. Thus, it allows the institutions of the European Union and the Member States to act on all new narcotic and psychotropic substances ([4]) that appear on the European Union drug market. The Council Decision also provides for an assessment of the risks associated with these new psychoactive

([1]) EMCDDA. (2010), *Risk assessment of new psychoactive substances: Operating guidelines*, Publications Office of the European Union, Luxembourg. Available at: http://www.emcdda.europa.eu/html.cfm/index100978EN.html

([2]) OJ L 127, 20.5.2005, p. 32.

([3]) The information exchange mechanism laid down by the Council Decision is operationalized as the *European Union Early Warning System on New Psychoactive Substances ('EU Early Warning System')*. It is operated by the EMCDDA and Europol in partnership with the Reitox National Focal Points and Europol National Units in the Member States, the European Commission, and the European Medicines Agency.

([4]) According to the definition provided by the Council Decision, a 'new psychoactive substance' means a new narcotic drug or a new psychotropic drug in pure form or in a preparation; 'new narcotic drug' means a substance in pure form or in a preparation that has not been scheduled under the 1961 United Nations Single Convention on Narcotic Drugs, and that may pose a threat to public health comparable to the substances listed in Schedule I, II or IV; 'new psychotropic drug' means a substance in pure form or in a preparation that has not been scheduled under the 1971 United Nations Convention on Psychotropic Substances, and that may pose a threat to public health comparable to the substances listed in Schedule I, II, III or IV.

substances so that, if necessary, control measures can be applied in the Member States for narcotic and psychotropic substances ([5]).

α-PVP was formally notified to the EMCDDA through the EU Early Warning System in April 2011 by France, in accordance with Article 4 of the Council Decision. The notification related to the seizure of approximately 5 kilograms of a white powder containing α-PVP and pentedrone which was seized by French customs authorities in February 2011. Following an assessment of the available information on α-PVP, and in accordance with Article 5 of the Council Decision, on 3 August 2015 the EMCDDA and Europol submitted to the Council of the European Union, the European Commission, and the European Medicines Agency (EMA), a *Joint Report* on α-PVP ([6]). Taking into account the conclusion of the *Joint Report*, and in accordance with Article 6 of the Council Decision on 15 September 2015, the Council formally requested that 'the risk assessment should be carried out by the extended Scientific Committee of the EMCDDA and be submitted to the Commission and the Council within twelve weeks from the date of this notification'.

In accordance with Article 6.2, the meeting to assess the risks of α-PVP was convened under the auspices of the Scientific Committee of the EMCDDA with the participation of four additional experts designated by the Director of the EMCDDA, acting on the advice of the Chairperson of the Scientific Committee, chosen from a panel proposed by Member States and approved by the Management Board of the EMCDDA. The additional experts were from scientific fields that were either not represented, or not sufficiently represented on the Scientific Committee, and whose contribution was necessary for a balanced and adequate assessment of the possible risks of α-PVP, including health and social risks. Furthermore, two experts from the Commission, one expert from Europol, and one expert from the European Medicines Agency (EMA), participated in the risk assessment. The meeting took place on 18 November 2015 at the EMCDDA in Lisbon. The risk assessment was carried out on the basis of information provided to the Scientific Committee by the Member States, the EMCDDA, Europol and the EMA. A list of the extended Scientific Committee, as well as the list of other participants attending the risk assessment meeting, is annexed to this report (Annex 2).

For the risk assessment, the extended Scientific Committee considered the following information resources:

i. Technical report on 1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one (α-pyrrolidinovalerophenone, α-PVP) (Annex 1);

([5]) In compliance with the provisions of the United Nations Single Convention on Narcotic Drugs of 1961 and the United Nations Convention on Psychotropic Substances of 1971.

([6]) EMCDDA and Europol. (2015), EMCDDA–Europol joint report on a new psychoactive substance: 1-phenyl-2-(1-pyrrolidinyl)-1-pentanone (α-PVP), EMCDDA, Lisbon. Available at: http://www.emcdda.europa.eu/publications/joint-reports/alpha-pvp

ii. EMCDDA–Europol Joint Report on a new psychoactive substance: 1-phenyl-2-(1-pyrrolidinyl)-1-pentanone (α-PVP) ([6]);

iii. Scientific articles, official reports, grey literature, internet drug discussion forums and related websites (hereafter 'user websites');

iv. Data from EMCDDA monitoring of internet vendors offering α-PVP (that typically appear to be manufacturers and/or wholesalers and/or retailers);

v. The EMCDDA operating guidelines for the risk assessment of new psychoactive substances ([1]); and,

vi. Council Decision 2005/387/JHA of 10 May 2005 on the information exchange, risk assessment and control of new psychoactive substances ([2]).

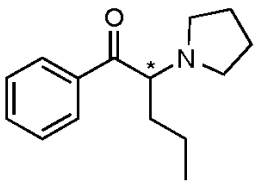
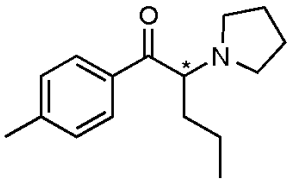
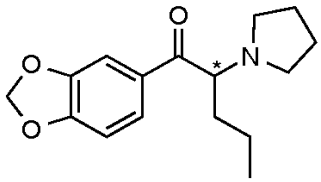
Finally, it is important to note that this risk assessment report contains a discussion of the available information on serious adverse events such as acute intoxications (typically presenting to hospital emergency departments) and deaths associated with α-PVP. Such information is critical to the identification of emerging toxicological problems associated with new psychoactive substances within the European Union. In this context, it is important to recognise that the capacity to detect, identify, and report these events differ both within and between Member States. In the past few years, programmes have been introduced in some Member States to strengthen these capacities. In addition, the EMCDDA's toxicovigilance system, which forms a central component of the EU Early Warning System, has also been strengthened. As a result, more information is available; however, it is likely that serious adverse events such as these remain under-detected.

2. Physical, chemical and pharmacological description

α-PVP is a pyrrolidine cathinone ([7]) derivative, where the nitrogen is part of a pyrrolidine ring and a propyl chain is attached to the alpha carbon. α-PVP shares these structural features with pyrovalerone and methylenedioxypyrovalerone (MDPV), both of which are psychostimulants controlled under the United Nations Convention on Psychotropic Substances of 1971 (Figure 1).

Figure 1. The molecular structure, IUPAC name, common name, molecular formula, molecular weight, and monoisotopic mass, of α-PVP. The structures of pyrovalerone and MDPV are provided for comparison. Chiral centres are denoted by an asterisk on the molecular structures.

([7]) Cathinone is a naturally occurring psychostimulant which is one of the psychoactive principles of the khat plant (*Catha edulis* Forsk). Cathinone is controlled under the United Nations Convention on Psychotropic Substances of 1971.

	**α**-PVP IUPAC name: 1-phenyl-2-(pyrrolidin-1-yl)pentan-1-one Common name: alpha-pyrrolidinovalerophenone Molecular formula: $C_{15}H_{21}NO$ Molecular weight: 231.34 Monoisotopic mass: 231.16231
	
Pyrovalerone	MDPV

The hydrochloride salt of **α**-PVP is described as a white, crystalline powder. Information provided from seizures and collected samples reported by the Member States have usually noted the presence of **α**-PVP in powder and tablet form.

α-PVP contains a stereogenic centre thus allowing for the existence of a pair of enantiomers: (*S*)-**α**-PVP and (*R*)-**α**-PVP. There is no information on the isomeric composition of the samples of **α**-PVP detected within the European Union; in part this may reflect the fact that stereochemical analysis is not routinely undertaken in forensic laboratories.

Analysis of **α**-PVP is straightforward with suitable equipment such as gas chromatography mass spectrometry (GC-MS), liquid chromatography mass spectrometry (LC-MS), Fourier transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR). Detection in biological matrices however may require the implementation of a more complex sample preparation procedure. The availability of analytical reference material is important for correct identification and for facilitating the quantification of **α**-PVP in physical samples and in biological matrices. Such reference materials are commercially available.

Route of administration and dosage

Typical routes of administration for **α**-PVP include nasal insufflation, injection (intravenous) and oral. Other routes have also been reported. Limited information from user websites suggests that a range of doses may be used and that these may depend on the route of administration. Self-reported user experiences have noted that in some individuals the 'threshold' level for **α**-

PVP (that is the dose required to induce an effect which the user can perceive) may occur with oral doses of 1–2 mg; 'strong' effects were reported with oral doses of 20–25 mg.

Pharmacodynamics

The available evidence indicates that α-PVP is a potent psychostimulant.

In vitro studies suggest that α-PVP acts predominantly as an inhibitor of dopamine (DA) uptake at the dopamine transporter (DAT) and norepinephrine (NE) uptake at the norepinephrine transporter (NET). This is a phenomenon that is also known to occur with other psychostimulants with monoamine uptake properties, such as MDPV. Importantly α-PVP does not inhibit serotonin (5-HT) uptake at the serotonin transporter (SERT), which is a similar finding to MDPV. Information about the pharmacology of the individual enantiomers of α-PVP has not been published. Information on the effect of α-PVP on other pharmacological targets is not available.

Information from animal studies suggests that the effects of α-PVP are similar to those observed with other psychostimulants such as MDPV, cocaine, and methamphetamine, where the roles of catecholaminergic mechanisms are well established. The neurochemical and behavioural features associated with α-PVP include locomotor activation, detection of increased levels of extracellular dopamine levels in mice striatum using microdialysis, and full substitution for the discriminative stimulus effects of cocaine and methamphetamine. Similar to MDPV, α-PVP was shown to act as a reinforcer when studied by conditioned place preference and using intravenous self-administration in rats.

Pharmacokinetics

Studies on the pharmacokinetics of α-PVP are limited to determination of metabolites. These studies have identified a number of metabolites including HO-α-PVP diastereomers, 2''-oxo-α-PVP, 2''-HO-α-PVP, and HO-α-PVP glucuronide. The pharmacology and toxicology of these metabolites is unknown.

There are no published data on the interaction of α-PVP with other substances, including other psychoactive substances and medicinal products.

Psychological and behavioural effects

Information from animal studies suggests that the acute behavioural effects of α-PVP might bear some similarities to other psychostimulants such as MDPV, cocaine, and methamphetamine.

There are no published data on the psychological and behavioural effects of α-PVP in humans. Limited information from acute intoxications and self-reported user experiences suggest that the effects of α-PVP might be broadly similar to other psychostimulant drugs such as MDPV.

Legitimate uses

α-PVP and its enantiomers are used in scientific research as well as analytical reference materials in clinical and forensic case work. There are currently no other indications that α-PVP may be used for other legitimate purposes. There are no reported uses of α-PVP as a component in industrial, cosmetic or agricultural products.

α-PVP does not appear to have an established or acknowledged medical value or use (human or veterinary) in the European Union. There is no marketing authorisation (existing, ongoing or suspended) for α-PVP in the European Union or in the Member States that responded to the information request by the EMA that was launched under Article 5 of the Council Decision ([6]). In addition, there is no information that α-PVP is used for the manufacture of a medicinal product or an active pharmaceutical ingredient of a medicinal product in the European Union ([6]). It is important to note that the data collection is incomplete and some countries indicated that this information is unknown. It should also be noted that there is no European Union database on the synthetic routes of all registered medicinal products. Therefore, the use of α-PVP cannot be ruled out with certainty.

3. Chemical precursors that are used for the manufacture

Currently there is no information regarding the chemical precursors, or the synthetic routes used for the α-PVP that has been detected on the drug market within the European Union.

Methods for the production of α-PVP are documented in the scientific literature. The production of α-PVP is relatively straightforward, in that it does not require a high level of technical expertise, training or complicated laboratory equipment. Typically, synthesis of cathinone derivatives can be completed at room temperature, requiring access to the appropriate starting materials and standard laboratory equipment. Methods documented include α-halogenation of 1-phenylpentan-1-one (valerophenone) followed by amination with pyrrolidine. Of note here is that the synthesis of cathinone derivatives in general can be completed using this particular route. Valerophenone is commercially available; it is not controlled under the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances of 1988. Valerophenone may also be obtained from a variety of other starting materials such as benzaldehyde. Benzaldehyde is commercially available; it is not listed under the 1988 Convention but is listed in the European Union voluntary monitoring list of non-scheduled substances. Other routes have also been reported and include the use of Grignard conditions, reaction of an epoxide intermediate with pyrrolidine, or involvement of the ephedrine-type precursor.

Detailed information regarding the presence of side-products or impurities arising from the synthetic process is not available. There is no quantitative data on impurities detected in drug samples from the European market. Nonetheless, the presence of route-specific impurities in samples of α-PVP is possible.

4. Health risks

Individual health risks

The assessment of individual health risks includes consideration of the acute and chronic toxicity of **α**-PVP, as well as its abuse liability and dependence potential. Similarities to, and, differences from, other chemically or pharmacologically related substances should also be considered.

It is important to note that when interpreting information from acute intoxications and deaths as well as information from user websites, individuals may have used other pharmacologically active substances in addition to **α**-PVP. The presence of and/or interaction with other substances may account for the effects reported.

The mode of use of **α**-PVP may involve the combined use of other drugs (either intentionally or unintentionally). This may be especially the case when **α**-PVP is encountered within powders offered and disguised in combination with other substances and ecstasy-type tablets. Analyses of various seized products have shown that the composition can differ and the user is unlikely to be aware of the exact dose or substance(s) being ingested (by whatever route) which presents an inherent risk to the individual.

Acute toxicity

The median lethal dose (LD_{50}) of **α**-PVP hydrochloride administered intravenously to mice is 38.5 mg/kg. No other studies were identified that investigated the acute health effects of **α**-PVP and/or its metabolites in animals.

No clinical studies were identified that have examined the acute health effects of **α**-PVP and/or its metabolites in humans.

Acute intoxications

205 acute intoxications associated with **α**-PVP were reported by eight Member States. These occurred between 2011 and 2015. Typically these cases related to acute presentations at hospital emergency departments. In 191 of these cases **α**-PVP was analytically confirmed in one or more biological sample taken from the patient. Case level data was available for 29 of these cases; 23 were non-fatal intoxications and in the remaining 6 cases the outcome was unknown.

Of these 29 cases, 24 were male and 4 were female; data on sex was missing for one case. The mean age of the male cases was 33.9 years (n = 21; median 32 years); data on age was missing for four male cases. The mean age of the female cases was 24.3 years (n = 4; median 24.5 years).

In about 50% of the cases other drugs, particularly benzodiazepines, were identified. Clinical features were generally consistent with sympathomimetic toxicity. These included: tachycardia, mydriasis, agitation or anxiety, tremor, hyperthermia, hallucinations, hypertension, diaphoresis, restlessness, convulsions or seizures. Of those cases where the route of administration was known, nasal insufflation, injection, and oral routes were reported.

Deaths

A total of 116 deaths associated with α-PVP were reported by eight Member States. These occurred between 2012 and 2015. In 115 of these cases, α-PVP was analytically confirmed in one or more biological sample taken from the decedents. Of these:

- in 23 (20%) cases, α-PVP was reported as the cause of death or was reported as a contributing factor (i.e. α-PVP was explicitly mentioned). This includes 5 (4%) cases where α-PVP was the only substance detected.
- In the remaining cases the cause of death was unknown or an alternative cause of death was reported. In the latter case, the manners of death were varied and included: hanging, drowning, fall, road traffic accident, carbon monoxide, blood loss, as well as cited drug intoxication.

In a majority of deaths, a wide variety of other substances were also detected. This included benzodiazepines, alcohol, opiates, opioids, antidepressants, and anticonvulsants. Of the other stimulants detected these included amphetamines, pseudoephedrine and synthetic cathinones (e.g. MDPV, pentedrone, 4-MEC, 3-MMC). Synthetic cannabinoids were also detected in some cases.

In all of the deaths there was a lack of information regarding the amount of α-PVP used, the route of administration, and any clinical features experienced prior to death. However, in those instances where clinical features have been described, tachycardia, hyperthermia, diaphoresis, agitation, convulsions or seizures, confusion, aggression, bizarre behaviour, and rhabdomyolysis were reported. Although other drugs were detected with most of these cases—including stimulants—the symptoms are generally consistent with those seen in acute intoxications.

Ability to operate machinery and drive

Any adverse behavioural effects of α-PVP may also extend to the ability to operate machinery and drive safely. Aggregated data related to cases of suspected driving under the influence of drugs (DUID) were reported to the EMCDDA. There are insufficient data available to discuss the circumstances of these cases. However, data suggests that stimulants can have detrimental effects on self-perception, critical judgement and risk-taking, and while the stimulating effects are wearing off the driver may suffer fatigue, anxiety and irritability.

Chronic toxicity

No studies were identified that investigated the chronic health effects of α-PVP and/or its metabolites in animals. No clinical studies were identified that have examined the chronic health effects of α-PVP and/or its metabolites in humans.

Abuse liability and dependence potential

No studies were identified that have investigated the abuse liability and dependence potential of α-PVP in humans. Data from *in vitro* and animal studies strongly suggest that α-PVP has abuse liability and possibly a dependence potential in humans.

Public health risks

The public health risks associated with α-PVP may be categorised in terms of patterns of use (extent, frequency, route of administration, etc.); availability and quality of the drug; information, availability and levels of knowledge amongst users; and, negative health consequences. Detailed information, including data on sporadic versus chronic use, that allow for a determination of public health risks associated with α-PVP are unavailable.

Extent, frequency, and patterns of use

There appear to be no data from general population surveys on the prevalence of α-PVP use. Data on the use of α-PVP within the European Union are limited to non-representative studies.

The available data suggests that α-PVP is used by recreational users and problem drug users. In the latter case this includes people who inject opioid and stimulant drugs, some of whom are attending low threshold harm reduction services and drug treatment services, including opioid substitution treatment services. The available data also suggests that polydrug use might be common in those using α-PVP.

Availability and quality on the market

α-PVP has been detected in all 28 Member States.

Data from seizures reported to the EMCDDA suggest that, in general, bulk quantities of α-PVP in powder form are mainly imported into the European Union from China. In addition to importation, two illicit production sites synthesising α-PVP have been seized in Poland; the α-PVP was intended for the domestic market and export. More than 750 kg of α-PVP in powder form has been seized in Europe since 2011. In most cases α-PVP has been seized as a powder, but other forms including tablets have been detected.

α-PVP is offered for sale in small, retail quantities (1 gram upwards) and in wholesale (kilogram) quantities by Internet retailers as a drug in its own right. The purity of these products may be claimed to be high but this has not been reported.

Detailed information available with regards to route-specific by-products produced during the synthesis of α-PVP is currently not available. There are no quantitative data available on the impurities detected in seized and collected samples reported to the EMCDDA by the Member States. Information on purity was only available for 17 seizures reported to the EMCDDA. Here the content of α-PVP ranged from 23% (2 seizures) to over 95% (8 seizures). In most cases, α-PVP was reported as the only active substance, although in about 35% of detections it was found in combination with other substances (predominantly stimulants). In these cases, quantitative analyses were not available.

Characteristics and behaviour of users

The available data suggests that α-PVP is used by recreational drug users and problem drug users. In the latter case, this includes people who inject opioid and stimulant drugs. Some of this group include individuals who are attending low threshold harm reduction services and drug treatment services, including opioid substitution treatment services. The data also suggests that polydrug use might be common in those using α-PVP. Further information on the size and demand and the characteristics of these groups of people is not available.

As noted, the available data suggests that α-PVP is used by problem drug users including those who inject stimulants and opioids. Drug injection is associated with health risks which include transmission of blood borne diseases. Injection of stimulant drugs has been associated with elevated levels of drug and sexual risk taking behaviours.

Nature and extent of health consequences

Data on the health consequences of α-PVP are mostly limited to the acute intoxications and deaths which are discussed above.

Long-term consequences of use

There is no information on the long-term consequences of α-PVP use.

Conditions under which the substance is obtained and used

It appears that α-PVP is sourced and used by individuals attempting to source the drug itself. Sources appear to include internet retailers, bricks-and-mortar shops, and street level drug dealers. In addition, some users may be unaware that they have sourced and used α-PVP either because they have obtained it as 'legal high' products with no indication that it contains α-PVP or because it has been mis-sold on the illicit market as a drug such as MDPV or methamphetamine, or sold as ecstasy.

Based on the available data, it appears that α-PVP is used in the same environments as other psychostimulants. This would be typically (but not restricted to) home environments, pubs/bars and discotheques/nightclubs, and outdoor music festivals. In addition, α-PVP is likely to be used

in some of the other environments used by problem drug users who inject opioids and stimulants.

5. Social risks

Data on the social risks of α-PVP are limited.

Individual social risks

There is no information on whether the use of α-PVP affects education or career, family or other personal or social relationships, including marginalisation.

Possible effects on direct social environment (e.g. neglect of family, violence)

There is no specific information on the possible effects of α-PVP on the direct social environment.

While there have been no clinical studies of the effects on α-PVP in humans, data from animal studies as well as from acute intoxications, deaths, and, self-reported user experiences, suggest that the acute behavioural effects of α-PVP might bear some similarities to other psychostimulants such as cocaine, methamphetamine, and MDPV.

Possible effects on society as a whole (public order and safety, acquisitive crime)

Data related to the social risk associated with the trafficking and distribution of α-PVP is limited. According to data provided by Europol, the seizure of two illicit production sites for α-PVP in Poland was linked to local football hooligans (Section 6). No further information is available.

Economic costs (demands on healthcare)

Due to the lack of data, it is not possible at this time to estimate whether α-PVP is associated with greater healthcare costs than other stimulant drugs.

Possible appeal to specific population groups

There is no specific data on the possible appeal of α-PVP to specific user groups. However, the available data suggests that α-PVP is used by recreational drug users as well as by problem drug users including those who inject stimulant and opioid drugs. Problem drug users are often marginalised. Overall, the extent of the possible appeal of α-PVP to these two broad groups of users is unknown.

6. Information on manufacturing, trafficking, distribution, and the level of involvement of organised crime

α-PVP has been available on the European Union drug market since at least February 2011. It

has been detected in all 28 Member States ([8]).

More than 750 kg of α-PVP in powder form has been seized in Europe since 2011. In most cases α-PVP has been seized as a powder, but other forms including tablets have been detected.

In terms of trafficking and distribution, it appears that bulk, multi-kilogram quantities of α-PVP are imported into the European Union from China and then distributed across Europe. This includes a single seizure of almost 260 kg in 2015. In addition to importation from China, two illicit production sites have been seized in Poland (in 2013 and 2014) where multi-kilogram quantities of α-PVP were synthesised. The synthesis was supervised by trained chemists, and the laboratories were supported by suppliers, producers and distributors of chemicals. The companies involved operated their own websites selling and distributing α-PVP across Poland. This case demonstrates that the capability to manufacture α-PVP exists within the European Union.

In respect to the processing of α-PVP in Europe, Hungary reported that α-PVP was detected in two tablet manufacturing sites which were dismantled in 2013 and in 2014, respectively. The site seized in 2013 was a tableting unit where pentedrone tablets were produced; 24,908 tablets containing pentedrone and 800 grams of α-PVP in powder form were seized. In 2014, a tablet manufacturing site where pentedrone tablets were produced was also dismantled; in the storage location linked to this site, 1.5 kg of α-PVP in powder form was seized. According to Hungarian police in both these cases the suspects intended to produce tablets using the α-PVP powder.

Limited information is available in relation to the involvement of organised crime in the manufacture and/or trafficking of α-PVP. Hungarian authorities reported that there are no established organised crime groups involved in the manufacture or trafficking of α-PVP. Latvian authorities reported that since 2014, a new trend has been observed in relation to the market in new psychoactive substances: a Latvian organised crime group was involved in the mixing and distribution of new psychoactive substances in herbal form and in one such case, the herbal substance was mixed with α-PVP.

Some of the seizures of tablets by law enforcement that contained α-PVP showed a range of colours, markings and logos ([9]) consistent with ecstasy tablets. This raises the possibility that some of these tablets may have been designed to be sold as ecstasy on the illicit drug market.

([8]) α-PVP has also been detected in Turkey and Norway.

([9]) It is common to find markings on tablets sold as ecstasy including those of popular cultural and iconic brands often having an association with quality.

7. Information on any assessment in the United Nations system

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 of 1961 and the Convention on Psychotropic Substances of 1971. At the time that the Joint Report ([6]) was prepared, the World Health Organization informed the EMCDDA that **α**-PVP was not currently under assessment nor had it been under assessment by the United Nations system. In November 2015, the World Health Organization informed the EMCDDA that **α**-PVP was assessed at the Thirty-Seventh meeting of the Expert Committee on Drug Dependence that was held 16–20 November 2015. The outcome of the assessment has not yet been published.

8. Description of the control measures that are applicable in the Member States

Sixteen Member States (Czech Republic, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Poland, Romania, Slovenia, Sweden, and the United Kingdom) reported that **α**-PVP is controlled under drug control legislation ([10]).

- In the Czech Republic, **α**-PVP has been listed in Government Regulation No. 463/2013 Coll., (as amended) since 1 October 2015.
- In Estonia, **α**-PVP has been listed in the Regulation No. 73 of the Minister of Social Affairs of 18 May 2005 since 2 June 2014.
- In Finland, **α**-PVP has been listed in the Narcotics Act 373 of 2008 since 30 December 2013.
- In France, **α**-PVP was added to the controlled narcotic substance list on 2 August 2012.
- In Germany, **α**-PVP has been placed under schedule II (narcotics eligible for trade but not for medical prescription) of the Narcotic Substance Act, effective as of 17 July 2013.
- In Greece, **α**-PVP is considered to be controlled under law 3459/2006 due to the fact that it has the same molecular weight and molecular formula as metazocine, an opioid analgesic classified in Table C of this law.
- In Hungary, **α**-PVP is listed in Schedule A (psychotropic substances) of Act XXV of 1998 on human pharmaceuticals since 1 January 2015.
- In Ireland, **α**-PVP is covered by the generic definition of controlled cathinones included in the Misuse of Drugs Act.

([10]) Turkey and Norway also reported that **α**-PVP is controlled under drug control legislation. In Turkey, **α**-PVP is listed in the Law on Control of Narcotics No. 2313 adopted on 22 March 2012. In Norway, **α**-PVP is covered by the generic definition of cathinones in the Norwegian list of narcotics.

- In Italy, α-PVP is also controlled generically, as a derivative of 2-amino-1-phenyl-1-propanone, under the Decree of the President of the Republic 309/90 since 29 December 2011.
- In Latvia, α-PVP is controlled generically according to Cabinet Regulation 847 'Regulations regarding narcotic substances, psychotropic substances and precursors to be controlled in Latvia'.
- In Lithuania, α-PVP is controlled as a cathinone derivative by an Amendment to the Law on the control of narcotic drugs and psychotropic substances adopted in 2010.
- In Poland, α-PVP is listed in Schedule IV of the Act of 24 April 2015 amending the Act of Counteracting Drug Addiction since 1 July 2015.
- In Romania, α-PVP is controlled by Law 143/2000 on preventing and combating trafficking and illicit drug use and it is listed in Table I of the law 339/2005 on the legal regime of plants, narcotic and psychotropic substances and preparations.
- In Slovenia, α-PVP was included by the Decree on amending the Decree on Classification of Illicit Drugs, Official Gazette of RS No. 45/2014 since July 2014.
- In Sweden, α-PVP comes under the Narcotic Drugs Control Act since 1 February 2013.
- In the United Kingdom, α-PVP was included in the generic definition of substituted cathinone derivatives placed under the Misuse of Drugs Act 1971 in April 2010.

Four Member States (Austria, Cyprus, Portugal, and Slovakia) reported that α-PVP is controlled under legislation prohibiting the unauthorised supply of defined or qualifying new psychoactive substances.

- In Austria, α-PVP is categorised as member of the 'amino phenyl ethanone' (i.e. cathinone) generic group in the new psychoactive substances act.
- In Cyprus, α-PVP also falls under the generic definition of a cathinone under specific NPS legislation as of 24 June 2011.
- In Portugal, α-PVP is listed as controlled under Decree-Law 154/2013 of 17 April 2013.
- In Slovakia, α-PVP is listed as a 'hazardous substance' as of 1 October 2013.

In the Netherlands, the sale of α-PVP in consumer amounts is treated as being a medicinal product and must comply with medicines legislation.

Seven Member States (Belgium, Bulgaria, Croatia, Denmark, Luxembourg, Malta, and Spain) reported that α-PVP is not subject to control measures at the national level. Belgium reported that they have started the process to control the substance under drug control legislation.

9. Options for control and the possible consequences of the control measures

Under Article 9.1 of the Council Decision, the option for control that is available at European Union level is for the Member States to submit the new psychoactive substance α-PVP to control measures and criminal penalties, as provided for under their legislation, by virtue of their obligations under the Convention on Psychotropic Substances of 1971. There are no studies on the possible consequences of such control measures on α-PVP. If this option of control is pursued, the Committee considers that the following consequences are possible. Some of these may apply to any new psychoactive substance.

- This control option could be expected to limit the availability of α-PVP and hence the further expansion of the current open trade in this substance.
- A health consequence that might result from this control option is the benefit brought about by the presumed reduction in availability and use. In this respect it is noteworthy that the People's Republic of China placed α-PVP under national drug control legislation on the 1 October 2015.
- This control option could facilitate the detection, seizure and monitoring of α-PVP related to its unlawful manufacture, trafficking and use. In so doing, it could facilitate cooperation between the judicial authorities and law enforcement agencies across the European Union.
- This control option would imply additional costs for the criminal justice system, including forensic services, law enforcement, and the courts.
- This control option could lead to replacement with other (established or new) psychoactive substances, which may in themselves have public health consequences and social risks.
- This control option could create an illicit market in α-PVP with the increased risk of associated criminal activity, including the involvement of organised crime.
- This control option could impact on both the quality/purity and price of any α-PVP still available on the illicit market. The extent to which this will impact on public health, criminality, or levels of use, is difficult to predict.
- It is difficult to predict the impact of this control option on current or future research by the pharmaceutical or chemical industries.
- In order to examine the consequences of control, the Committee wishes to note that it will be important to monitor for the presence of α-PVP on the market post-control, should this control option be pursued.
- Aside from the option for control under those stipulated in Article 9.1 of the Council Decision, other options for control may be available to Member States. These may include restricting the importation and supply of the substance as some Member States have already done.