ACMD

Advisory Council on the Misuse of Drugs

Synthetic cathinones: an updated harms assessment

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Contents

List of figures

List of tables

1 Introduction

1.1. Synthetic cathinones are human-made stimulants chemically related to cathinone, one of the naturally occurring psychoactive principals that can be extracted from the khat plant (Catha edulis) (ACMD, 2010). The chewing of khat for its stimulant effects has been common for centuries amongst communities from the horn of Africa and the Arabian Peninsula, where the plant is endemic. However, this practice has not become popular in Europe due to the challenges in obtaining the fresh product, the duration of chewing needed to obtain a psychoactive effect and the bitter taste of the leaves. It is also easier and less expensive to manufacture synthetic cathinones in a laboratory than to extract psychoactive compounds directly from the khat plant.

1.2. Cathinone is structurally very similar to amphetamine (1-phenylpropan-2-amine), being its β-keto analogue. Most synthetic cathinones are modified by substitution in the aromatic ring, N-alkylation, or through the substitution of the alpha-carbon (EMCDDA, 2023). The chemistry of these compounds is discussed later in this report.

1.3. The prevalence of synthetic cathinone use in the UK increased sharply during the mid to late 2000s, as a cheaper, more accessible, and initially legal alternative to illicit drugs like cocaine and amphetamines. Examples encountered frequently at that time included 3,4-methylenedioxy-*N*-methylcathinone (MDMC, methylone), 3,4-methylenedioxypyrovalerone (MDPV), and especially mephedrone (4-methyl-*N*-methylcathinone or 4-MMC) (ACMD, 2010; Soares and others, 2021). These compounds were initially widely available for purchase, often mislabelled as ‘not for human use’ and sold online using misleading terms, such as ‘bath salts’, ‘plant food’ and ‘research chemicals’ (Karila and others, 2015). Use was commonly by swallowing, nasal insufflation, or smoking, with intravenous administration less common.

1.4. In view of their increasing prevalence at that time, the Advisory Council on the Misuse of Drugs (ACMD) provided advice on the use and harms of synthetic cathinones in 2010. Following the ACMD’s recommendations, the then government controlled synthetic cathinones as Class B substances under the Misuse of Drugs Act (MDA) 1971 (ACMD, 2010). A generic definition (a description of relevant chemical structures) was recommended, rather than controlling individual examples by name, because of the likelihood of potentially psychoactive variants emerging as a result of small chemical modifications. It therefore seemed likely that control of compounds by name could easily be circumvented.

1.5. Subsequently (and as predicted), large numbers of new synthetic cathinones have been reported in illicit drug markets. The European Monitoring Centre for

Drugs and Drug Addiction (EMCDDA)[1] was monitoring 162 examples by the end of 2021, making synthetic cathinones the second largest category of novel psychoactive substances (NPSs) under surveillance (after synthetic cannabinoids). In 2019, 222 separate synthetic cathinones were identified by combining information from the EMCDDA, the United Nations Office on Drugs and Crime (UNODC) database and cathinones mentioned in a range of psychonaut, NPS-related, online sources collected using web crawler software (Schifano and others, 2020). Most of these emerging compounds were captured by the original UK generic definition, but substances have occasionally been encountered that evade this control (Kuropka and others, 2023a).

1.6. Understanding of the synthetic cathinones in circulation is further complicated by complex abbreviations and the range of synonyms used in different publications. In this report, a consistent approach to nomenclature is used, with synonyms and abbreviations defined in Annex A, where selected chemical structures are also provided.

1.7. Synthetic cathinones may produce euphoria and increased alertness when used in low doses. However, dose-related adverse effects may also occur, including nausea and vomiting, agitation, confusion, palpitations, tachycardia, chest pain, and hypertension. Less commonly, convulsions, hyperthermia, hallucinations, rhabdomyolysis, ECG abnormalities, headaches, skin rashes and peripheral vasoconstriction may occur. Users of synthetic cathinones self-report feelings of euphoria, hallucinations, involuntary body movements, confusion, anxiety, psychosis, and depression (Pieprzyca and others, 2022).

1.8. Like other psychostimulants (such as amphetamine), synthetic cathinones act by impairing the normal function of plasma membrane transporters in the central nervous system of the neurotransmitters dopamine (DAT), norepinephrine, (NET) and serotonin (SERT), transporters that belong to the solute carrier 6 (SLC6) family. The result is increased concentrations of these neurotransmitters at their site of action in the synaptic cleft (Nadal-Gratacós and others, 2024). Some evidence shows that separate groups of cathinones can have dissimilar pharmacological effects, and that these could result in more marked harms after human use. The pharmacology of these compounds is discussed in detail in Section 6 of this the report.

1.9. Particular concerns have been raised about a substance colloquially known as ‘monkey dust’, a term used to describe a street product that can contain several different synthetic substituted cathinone compounds, in particular 3',4'-methylenedioxy-α-pyrrolidinohexiophenone (MDPHP). This is one of several compounds that are termed pyrrolidino-cathinones in this report, but may also be referred to elsewhere as pyrovalerones, α-pyrrolidinophenone derivatives, or (in online fora) as ‘pyros’ (Pulver and others, 2023). Use of ‘monkey dust’ has most often been reported from North Staffordshire and its

[1] The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) has recently changed its name to the European Union Drugs Agency (EUDA).

environs, where it is reported to be associated with severe clinical effects and a negative impact on local communities.

1.10. In May 2023, the then Minister of State for Crime, Policing and Fire commissioned the ACMD for an updated harms assessment of synthetic cathinones, noting an apparent increase in reports of use and harms of these drugs. The commissioning letter also requested advice on whether those compounds that are sold as ‘monkey dust’, including MDPHP, are significantly more harmful than other synthetic cathinones and may therefore require a separate approach (Home Office, 2023).

1.11. This review has therefore been conducted to examine the current illicit use of synthetic cathinones in the UK with the aims of:

- identifying the specific compounds causing health and social harms in the UK, including examples that are not captured by the current generic definition for cathinones
- documenting the pharmacology, health and social harms of compounds of concern
- considering whether certain synthetic cathinones are significantly more harmful than others and require a different classification under the MDA 1971

Background

2 Legitimate use

2.1. Several synthetic cathinones are, or have been, licensed as human medicines in the UK or internationally, as follows:

a) Bupropion (formerly called amfebutamone) is currently licensed as an aid to smoking cessation in the UK and elsewhere (Zyban®). There is also a bupropion preparation licensed to treat depression (Wellbutrin®) and a combination preparation with naltrexone (Mysymba®) licensed in the UK for management of weight in adults with high body mass index.

b) Pyrovalerone was previously an approved medication in the USA, France and Spain, although seldom prescribed and associated with abuse and dependence. It is not licensed as a medicine in the UK.

c) Diethylpropion (amfepramone, Tenuate Dospan®) was previously licensed in the UK as an appetite suppressant for weight reduction but is no longer licensed or listed in the British National Formulary. It is, however, prescribed as a 'special' by some weight loss clinics and can apparently also be obtained from online pharmacies.

2.2. The Medicines and Healthcare products Regulatory Agency (MHRA) have confirmed there are no licensed or pending licensing applications for products containing any of the cathinones listed in Annex A. No seized medicines have been encountered that tested positive for the presence of any of the listed cathinones since the relevant database was initiated in 2013.

2.3. The ACMD is not aware of legitimate use for other synthetic cathinones, except as reference standards for laboratory analysis.

3 Current legal status

United Kingdom

3.1. Some cathinones were controlled under the MDA prior to 2010 and are listed in the Misuse of Drugs Regulations (MDR) 2001 Schedules as follows:

- cathinone (Class C, Schedule 1)
- methcathinone (Class B, Schedule 1)
- pyrovalerone (Class C, Schedule 4 part 1)
- diethylpropion (Class C, Schedule 3)

3.2. Cathinone and methcathinone were placed in Schedule 1 of the MDR as they were considered to have no medicinal use. Pyrovalerone and diethylpropion were placed in Schedule 4, part 1 and Schedule 3, respectively, because they had previously been licensed as medicines, either in the UK or in other countries.

3.3. The ACMD considered khat in 2013 and did not recommend control (ACMD 2013), but the then government decided to place it in Class C of the MDA, with the aim of protecting vulnerable members of communities and discouraging its illegal international trafficking. It was also listed in Schedule 1 of the MDR.

3.4. When, after 2008, cathinones began to emerge as stimulant NPS, it was clear that the chemical backbone provided numerous opportunities for variation and the potential for many new synthetic cathinones to be synthesised. As a result, control of these compounds using individual compound names was likely to be unsuccessful due to the emergence of new synthetic cathinones. The ACMD therefore previously advised that a generic definition was a more future-proof approach.

3.5. Four broad categories of cathinones were identified, based on chemistry:

(i) simple cathinones based on a phenyl ring with an alkyl side chain with both an oxygen atom on the side chain at the position adjacent to the ring and an amine group attached to the next carbon atom of the chain;

(ii) variants with the simple structure modified by the addition of a methylenedioxy group to the phenyl ring;

(iii) materials with the nitrogen of the amine group incorporated into a five-membered pyrrolidine ring;

(iv) materials with both the methylenedioxy- and pyrrolidino- modifications.

3.6. The UK generic control was therefore developed to cover these structures, based on the 'model compound', 2-amino-1-phenyl-propan-1-one, combined with a specified list of modifications to the phenyl ring, alkyl additions to the propyl sidechain and either alkyl substitutions at the amine nitrogen or inclusion of the amine nitrogen into a cyclic structure.

3.7. This generic definition came into effect in April 2010 by means of SI 2010/1207.[2] However, it rapidly became apparent that the scope of the generic was insufficient when materials such as naphyrone (naphthyl pyrovalerone) appeared, where the phenyl ring had been replaced by a naphthyl structure to produce a potent stimulant. A second generic was therefore added to cover materials where the phenyl ring has been replaced by another monocyclic or polycyclic ring system. This expansion came into effect in July 2010 by means of SI 2010/1833. The generic controls have not been modified since 2010 and are detailed in Annex D.

3.8. Consequent to this generic definition, synthetic cathinones that had not previously been controlled were now classified as Class B under the MDA in 2010. Class B was recommended because the harms associated with synthetic cathinones encountered at that time, including mephedrone, were considered commensurate with those of the closely related compound amphetamine, which was already in Class B. They were also placed in Schedule 1 of the MDR because they were considered as having no legitimate medicinal use. Of note, there are also some related substances in Class A (methamphetamine, MDMA) and others in Class C (cathinone, pyrovalerone, khat, diethylpropion).

3.9. Bupropion is specifically excluded from the generic text concerning cathinones in the MDA and is therefore not a controlled drug in the UK. As a medicinal substance, it is also excluded from the provisions of the Psychoactive Substances Act (PSA) 2016. Although there have been international reports of misuse, bupropion is not considered further in this report.

3.10. The UK generic text has been successful in capturing most synthetic cathinones that have appeared on international drug markets since it became law. During the 16 years from 2008 to 2023, the EMCDDA (now called the European Union Drugs Agency or EUDA) issued 166 notifications of cathinone-type NPS and only 19 of these fall outside the scope of the current UK generics (see Annex A). Those non-medicinal synthetic cathinones that are psychoactive but not captured by the generic text are, however, subject to

[2] Statutory instruments (SI) are the principal form of delegated or secondary legislation in the UK.

the PSA. Details of the uncontrolled synthetic cathinones detected in the UK are provided later in this report.

International

3.11. As of 2024, 19 synthetic cathinones have been named in the list of materials covered by the 1971 United Nations (UN) Convention on Psychotropic Substances (the 'Green List'). All nations that are signatories to the UN Drug Conventions must take appropriate steps control listed materials through their national legislation, with the level of control reflecting their UN scheduling. Details of these compounds are provided in Annex B.

3.12. As the number of cathinone NPS identified has continued to expand, many countries have chosen to control other named cathinones beyond those on the UN's list. In addition, as the number of cathinone NPS has increased, some countries have adopted strategies to control groups of cathinones without having to individually list the chemicals. Several have enacted broad generic (structure-based) controls to cover numbers of substances, similar to that used in the UK, including Germany, France, Norway, Japan and Switzerland.

3.13. The level of control applied to different cathinone NPS within a nation's legislation tends to be standard across materials, rather than particular substances being subject to different levels of control. The only exceptions to this are those materials that have accepted medical applications, such as pyrovalerone and diethylpropion, which have been allocated lower levels of control. Further details of international controls are provided in Annex B.

4 Current UK prevalence

4.1. The prevalence of synthetic cathinones use in the UK was studied using published literature and information available online. In addition, ACMD wrote to a range of stakeholders in April 2024, including public health authorities, forensic service providers and academic researchers. Quantitative information was requested about synthetic cathinones recently identified in drug seizures by law enforcement or customs staff, submitted sample analysis, samples from those attending emergency departments with drug toxicity and forensic analysis of drug-related deaths.

4.2. The Crime Survey for England and Wales (CSEW) is an annual study asking members of the public living in households in England and Wales about their experiences of crime over the previous 12 months. Those aged 16 to 59 years are also asked questions on drug use. The CSEW has measured reported mephedrone use since the year ending March 2011, but does not request information about the use of other synthetic cathinones (ONS, 2024). Reductions in reported mephedrone use by adults aged 16 to 59 years, and also in the subgroup aged 16 to 24 years, have been documented over the last decade, from peaks in years ending March 2014 and 2015 (Table 1).

Table 1. Percentages of respondents aged 16 to 59 and 16 to 24 reporting mephedrone use in the last year, April 2010 to March 2023

Reporting year (April to March)	2010-11	2011-12	2012-13	2013-14	2014-15	2015-16	2016-17	2017-18	2018-19	2019-20	2022-23	2023-24
16 to 59 years	1.3	1.0	0.5	0.6	0.5	0.3	0.1	0.1	0.0	0.0	0.0	0.1
16 to 24 years	4.4	3.3	1.6	1.9	1.9	0.9	0.3	0.2	0.0	0.2	0.0	0.2

Note: The survey was not conducted for the years ending March 2021 and 2022 (ONS, 2023).

4.3. NHS Digital provides information on reported drug use from their periodic surveys of school pupils in school years 7 to 11 in England and Wales. This involves children and young people who are mostly aged 11 to 15 years (NHS England, 2022). Reported use of mephedrone declined in boys and girls between 2012 and the most recent survey in 2021 (Table 2). Use of other synthetic cathinones is not documented in this survey.

Table 2. Reported mephedrone use in school pupils (school years 7 to 11) in England and Wales (% respondents)

Reporting year	2012	2013	2014	2016	2018	2021
Boys	0.9	0.7	0.5	0.5	0.3	0.2
Girls	0.6	0.5	0.5	0.2	0.2	0.1

Source: NHS England (2022)

4.4. Stakeholders' responses to ACMD's data request in April 2024 are detailed in Annex C. The total numbers of synthetic cathinone detections reported from across the UK for the years ending March 2020 to 2023 are summarised in Table 3, with compounds ranked by frequency of detections overall in seized samples, submitted samples, emergency department (ED) patient toxicology and post-mortem (PM) toxicology. Overall, 71 different synthetic cathinones were detected in these various samples; analyses where exact structures could not be determined were not counted (such as chloromethcathinone (CMC), methylmethcathinone (MMC), chloroethcathinone (CEC) or methylethcathinone (MEC)).

4.5. Involvement in drug-related deaths is an important measure of health harms, although detection of a compound does not necessarily mean that compound was responsible for the death. The available data demonstrate that, in most cases, deaths involving a synthetic cathinone also involved other psychoactive substances. There is also an inevitable overlap between death registrations and PM toxicology findings when both have been provided from the same devolved administration. As data are anonymised, it is not possible to exclude double counting in some cases.

4.6. Mephedrone remains the most detected synthetic cathinone in seized samples, submitted samples, ED patient toxicology and drug-related deaths. There were also deaths where a methylmethcathinone was detected, but the precise structure (2-, 3- or 4-MMC) was not determined. Compounds where this is the case are labelled ‘not specified’ in this report. Many of these MMC (not specified) compounds were probably 4-MMC (mephedrone).

4.7. Excluding mephedrone and MMC (not specified), the synthetic cathinones most commonly implicated in drug-related deaths were MDPHP, α-PHP, α-PVP and dibutylone. Of those compounds for which adequate data are available, there was a higher ratio of detections in PM samples compared to detections in seizures or submitted samples for α-PHP and α-PVP compared to mephedrone and MDPHP. This might suggest that these compounds carry a higher risk of fatal outcome, but the data are difficult to interpret, because the numbers involved are relatively small, detections in seizures or submitted samples do not necessarily reflect prevalence of use in the population, and deaths where compounds are detected at PM may be caused by co-used drugs. Nevertheless, further review of the pharmacology, health and social harms of each of these compounds is appropriate.

4.8. Other compounds detected in more than one, but less than 5, drug-related deaths were eutylone, MEC (not specified), ephylone, pentylone, methylone and methedrone. All these compounds are controlled in Class B of the MDA, and further detailed review is not considered necessary at this time.

4.9. There were several commonly detected substances that were infrequently implicated as causes of death. These included 3- or 4-chloromethcathinone (CMC) or CMC (not specified), 3-MMC, *N*-ethyl hexedrone, dipentylone, 4-CEC, ethcathinone and α-pyrrolidinoisohexanophenone (α-PiHP). All these substances are currently controlled in Class B of the MDA, and further review of them is not warranted at this stage.

4.10. Longer-term data on suspected drug-related deaths involving synthetic cathinones are available from ONS. This demonstrates reductions since 2015, driven by reductions in those involving mephedrone. Numbers of deaths involving other cathinones have not reduced substantially, but make up a very small component of overall drug-related deaths.

4.11. Further detail on time trends affecting specific cathinones involved in drug-related deaths is available from the National Programme on Substance Use Mortality (NPSUM). Consistent with data from the ONS, deaths involving mephedrone have fallen substantially since 2015, but there have also been reductions for other synthetic cathinones more commonly implicated in drug-related deaths, specifically α-PVP since 2016, MDPHP since 2018, dibutylone since 2020 and α-PHP since 2021. This information, however, should be interpreted with caution because the numbers involved are small. There are also delays between a death and conclusion of the relevant coronial inquest, so data for the most recent years in particular are likely to be incomplete.

4.12. There were 7 compounds detected between 2019 and 2023 that are currently not controlled in the UK via the MDA, specifically mexedrone, BMDP, α-D2PV,

N-cyclohexylnormethylone, N-cyclohexylnorbutylone, *N*-methylbenzedrone and benzedrone. Of these, only mexedrone and benzedrone were detected in PM toxicology samples and only in one case each. Eurofins have also reported detection of an eighth uncontrolled cathinone during 2024, *N*-cyclohexylmethylone. Further review of these compounds, alongside others detected in Europe but not so far in the UK, is therefore necessary.

Table 3. Reported detections of synthetic cathinones in the UK, years ending March 2020 to 2023, ranked by totals overall

	Submitted samples[1]	Seized samples[2]	ED samples[3]	PM toxicology[4]	Overall total
Mephedrone	318	1,495	31	49	**1,893**
4-CMC	180	789	5	1	**975**
MDPHP	0	732	0	32	**764**
α-PHP	12	484	0	43	**539**
3-MMC	55	239	0	1	**295**
Eutylone	20	262	6	5	**293**
Ephylone	24	148	7	2	**181**
N-Ethylhexedrone	4	134	1	0	**139**
Dipentylone	37	101	0	0	**138**
CMC (not specified)[5]	35	94	0	0	**129**
α-PiHP	0	125	0	0	**125**
3-CMC	14	78	0	0	**92**
α-PVP	10	71	3	7	**91**
Mexedrone*	9	78	0	1	**88**
4-CEC	14	60	0	1	**75**
Ethylone	23	38	0	1	**62**
MMC (not specified)	8	48	0	4	**60**
BMDP*	1	57	0	0	**58**
MDPEP	0	52	0	0	**52**
Methedrone	0	42	0	3	**45**
2-MMC	1	36	0	0	**37**
4-CDMC	0	28	0	0	**28**
N-Cyclohexylnormethylone*	0	27	0	0	**27**
Dibutylone	6	12	0	9	**27**
4F-3-Methyl-α-PVP	15	12	0	0	**27**
CEC (not specified)[5]	3	24	0	0	**27**
N-Ethylpentedrone	2	24	0	0	**26**
4-Cl-α-PPP	0	26	0	0	**26**
Ephedrone	0	24	2	0	**26**

	Submitted samples[1]	Seized samples[2]	ED samples[3]	PM toxicology[4]	Overall total
Methylone	2	19	0	2	**23**
Ethcathinone	0	20	0	0	**20**
N-Ethylheptedrone	14	6	0	0	**20**
4-MEC	0	18	0	0	**18**
Naphyrone	0	15	0	0	**15**
MDPV	0	12	0	3	**15**
Pentylone	2	9	2	1	**14**
4-MPHP	0	14	0	0	**14**
N-Butylhexedrone	2	9	0	0	**11**
4-MEAP	3	6	0	0	**9**
4F-α-PVP	0	8	0	0	**8**
N-Butylpentylone	1	7	0	0	**8**
4F-3-Methyl-α-PHP	1	7	0	0	**8**
N-Propylbutylone	0	5	0	0	**5**
TH-PVP	0	4	0	0	**4**
Tertylone	0	4	0	0	**4**
MEC (not specified)[5]	0	4	0	0	**4**
Normephedrone	3	1	0	0	**4**
4-Cl-α-PVP	0	4	0	0	**4**
Benzedrone*	0	2	0	1	**3**
α-D2PV*	1	2	0	0	**3**
3-FMC	0	3	0	0	**3**
EMC (not specified)[5]	0	3	0	0	**3**
MPBP	2	1	0	0	**3**
4-MP	0	3	0	0	**3**
N-Cyclohexylnorbutylone*	0	2	0	0	**2**
Propylone	0	2	0	0	**2**
Butylone	0	0	0	2	**2**
MDO-PPP	0	2	0	0	**2**
α-PNP	0	2	0	0	**2**
4-Fluoropentedrone	0	2	0	0	**2**
Flephedrone	0	2	0	0	**2**
N-Methylbenzedrone*	0	1	0	0	**1**
3-CEC	0	1	0	0	**1**
4F-PV8	0	1	0	0	**1**
α-PBP	0	1	0	0	**1**
Brephedrone	0	0	1	0	**1**

	Submitted samples[1]	Seized samples[2]	ED samples[3]	PM toxicology[4]	Overall total
3-MEC	0	1	0	0	**1**
4-methylcathinone	0	1	0	0	**1**
4F-α-PHP	0	1	0	0	**1**
MDPBP	0	1	0	0	**1**
NiPP	0	1	0	0	**1**
N-Methylmethedrone	0	1	0	0	**1**
Pentedrone	1	0	0	0	**1**
Buphedrone	0	1	0	0	**1**
Dimethylone	0	1	0	0	**1**
N-Ethylhexylone	0	1	0	0	**1**

Notes:

Abbreviations are defined and synonyms provided in Annex A.

Due to the anonymised nature of returns, duplication arising as a result of data from the same case appearing in more than one data set cannot be excluded.

*Compounds not covered by current generic text.

[1] Data from OHID, Eurofins, MANDRAKE, Border Force, FSNI (Drivers, drug and criminal samples), EDAT (previously FEWS), PHS (Prisons) and SPA.

[2] TICTAC and WEDINOS.

[3] IONA, ASSIST and NPIS telephone enquiries.

[4] ONS, EU-MADNESS, FSNI, NPSUM, SPA and PHS.

[5] 'Not specified' indicates that precise structure not determined

5 Chemistry

5.1. Synthetic cathinones are derivatives of the natural substance cathinone. The general structure of the synthetic cathinones is illustrated in Figure 1. They are structurally related to the amphetamines, but possess a carbonyl (keto) group at the β-position of the side chain (the benzylic carbon). A variety of synthetic methods are available to make cathinones. These are amenable to variation, so cathinones can be modified readily at 3 positions within the core structure – at the aromatic ring (X), the side chain (R) and at the amino group (R' and R", Figure 1).

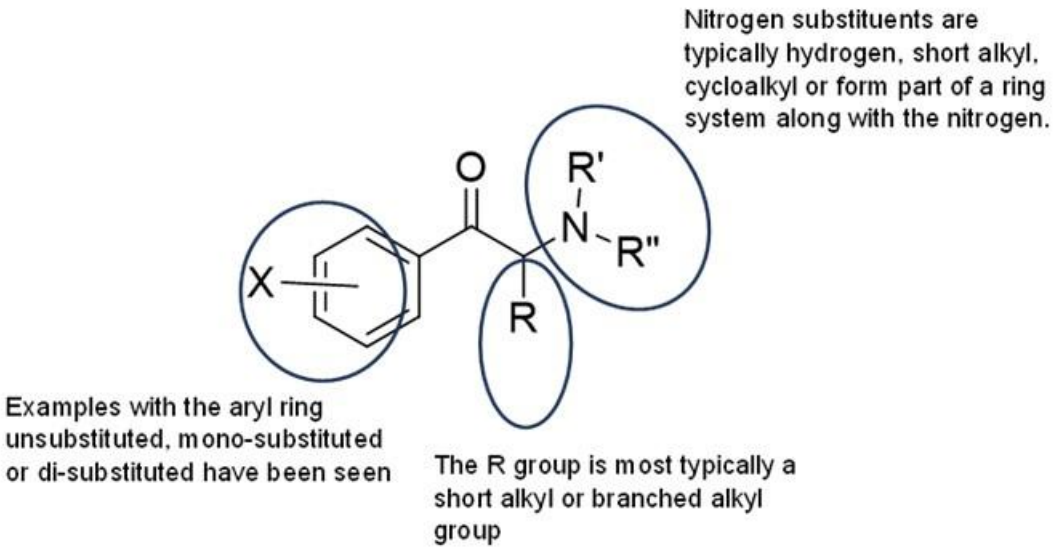


Figure 1. The general chemical structure of synthetic cathinones, highlighting the 3 positions within the core structure that can be modified easily

5.2. Due to the presence of a chiral centre, they can exist in 2 stereoisomeric (mirror image) forms, each of which might have a different pharmacology. Current routine testing does not differentiate these isomeric forms, although it is assumed that illicitly produced cathinones are found as racemic mixtures (that is, containing equal amounts of each stereoisomer).

5.3. At the time of the ACMD's 2010 report, the known cathinones were limited to those with no aromatic ring substituent or a single substituent (the exception being those with a methylenedioxy group). More recently, analogues have appeared where the substituent is attached to a different position of the ring (such as 2-Me-α-PVP), or where there are 2 discrete substituents (such as MFPHP). There is now also more variation in the alkyl side chain, with branched chain analogues appearing (such as 3F-α-PiHP) and even replacement of the alkyl side chain with aryl (such as α-D2PV). Likewise, evolution of the *N*-substituents continues with increased length (such as *N*-butylpentylone; 3-methyl-*N*-propylcathinone; *N*-propylbutylone), the appearance of piperidine rings (such as in α-piperidinobutiophenone (α-PipBP)), and cycloalkyl substituents (*N*-methyl-*N*-cyclohexymethylone, *N*-cyclohexylnormethylone, *N*-cyclohexylnorbutylone) (Kuropka and others, 2023b).

5.4. The synthetic cathinones most commonly identified in forensic analysis of drug-related deaths in the UK over the past 5 years were mephedrone, MDPHP, α-PHP and α-PVP. The latter 3 compounds emerged after publication of the previous cathinones report (ACMD, 2010), being reported in Europe in 2011 (α-PVP) and 2014 (MDPHP, α-PHP), but they are covered by the generic definition that was adopted at that time.

5.5. Some compounds that have emerged since 2010, however, are not covered by the current UK generic text definition and would require the generic to be updated if the compounds affected are considered as posing an actual or

potential risk. For example, analogues where the side chains or the nitrogen have an aryl or cycloalkyl group attached are not currently covered. These substituents can be further modified, potentially giving rise to a range of further variants. Compounds that are not covered by the current generic description are discussed later in this report.

6 Pharmacology and toxicology

6.1. Like other psychostimulants (such as amphetamine), synthetic cathinones act as central nervous system stimulants by increasing concentrations of the monoamine neurotransmitters dopamine, norepinephrine and (often to a lesser extent) serotonin at their site of action in the synaptic cleft, thus increasing their effects (Simmler and others, 2013; Karila and others, 2015; Baumann and others, 2018). They achieve this by one of the following actions (Nadal-Gratacós and others, 2024):

a) Blocking their reuptake from the synapse into the body of the neurone (nerve cell) by specific transporter proteins termed DAT, NET and SERT for dopamine, norepinephrine and serotonin respectively (see Figure 2A). Reuptake reduces the concentration of these neurotransmitters at their site of action in the synaptic cleft and is the natural process by which their actions are terminated. Compounds that block reuptake ('blockers') therefore prolong and increase the stimulant effects of the affected neurotransmitters. Examples include the pyrrolidino-cathinones such as MDPV, which are much more potent blockers of DAT than SERT (low SERT:DAT ratio). A low SERT:DAT ratio has been suggested to lead to increased psychostimulant effects and misuse liability (Luethi and Liechti, 2020; Negus and Banks, 2017), but this is not always the case.

b) Stimulating the release of neurotransmitters, thus increasing concentrations at their site of action in the synaptic cleft (see Figure 2B). Compounds with this action ('substrates' or 'releasers') bind to the transporter protein, are subsequently translocated into the cell body, and then trigger neurotransmitter release by reverse transport (Reith and others, 2015; Sitte and Freissmuth, 2015). Synthetic cathinones might also affect the intracellular vesicular monoamine transporters (for example, the vesicular monoamine transporter 2, or VMAT2) that regulate the amount of transmitter found in the vesicles or intracellular space (Magee and others, 2020). Examples of synthetic cathinones with this property include mephedrone and methylone. These compounds have a higher SERT:DAT ratio and are reported to have psychological effects more similar to MDMA.

c) Some compounds exhibit both of these actions, being DAT and NET reuptake inhibitors, but also dopamine and norepinephrine releasing agents (Glennon and Dukat, 2017). Examples are cathinone and methcathinone.

6.2. The processes of blocking uptake and promoting release are illustrated for dopamine in Figure 2. The pharmacological effects that result will depend on

the type of action involved (blocking, releasing, or both) and the relative potency of effects on the transporter proteins DAT, NET and SERT. The selectivity, or lack thereof, between monoamine systems means individual synthetic cathinones can have substantially different pharmacological profiles and clinical effects (Gonçalves and others, 2019). For example, compounds that act specifically on DAT and NET often have potent stimulant and dependency producing effects.

6.3. It should be noted that while the literature often describes some groups of cathinones as "cocaine-like", it is important to note that cocaine has very similar potency at all 3 uptake sites (DAT, NET and SERT), whereas very few cathinones match this profile. It should also be acknowledged that synthetic cathinones have very complex pharmacology and for many more recently encountered compounds there is limited information available about their specific cellular effects (Glennon and Dukat, 2017). The description above is a simplification and other factors are likely to contribute to their pharmacological actions (see below).

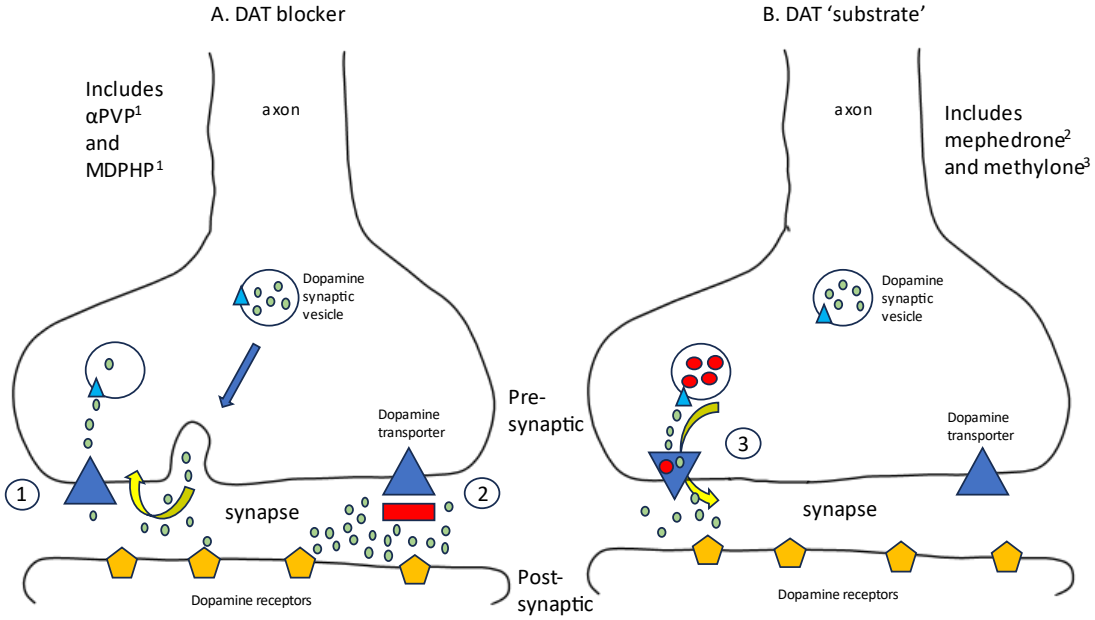


Figure 2. The dopamine synapse and effects of different DAT compounds on dopamine dynamics

Notes:

A. Dopamine synapse showing normal dopamine release after an action potential (1). Dopamine (small green circles) is packaged in synaptic vesicles. After an action potential, the vesicles merge (blue arrow) with the pre-synaptic membrane, releasing dopamine into the synapse. Dopamine can activate post-synaptic dopamine receptors (orange pentagons) and then is taken back up by the dopamine transporters (large blue triangles) and repackaged into synaptic vesicles by the vesicular monoamine transporter (small light blue triangle). When cocaine is present ((2) red rectangle), the dopamine transporter is

blocked, and the released dopamine accumulates in the synapse. This leads to overactivation of the post-synaptic dopamine receptors.

B. Amphetamine (small red circle) acts as a dopamine transporter substrate, it can be taken up by the dopamine transporter and the vesicular monoamine transporter, displacing dopamine from the vesicles. Dopamine then moves through the dopamine transporter, down its concentration gradient, into the synapse (3). The curved yellow arrows show the direction of dopamine movement (Baumann and others, 2013; Kolaczynska and others, 2021; Sahai and Opacka-Juffry, 2021).

6.4. The desired effects in humans (stimulant, hedonic) and the adverse effects (for example, agitation, delusions, paranoia, psychosis, seizures) appear consistent with the actions of synthetic cathinones on monoamine systems and consistent with behavioural studies in animals (Daziani and others, 2023).

6.5. Clinical effects in human users depend on:

a) The specific compound taken, its function (‘releaser’ or blocker’), its potency for interaction with the various monoamine transporter systems (DAT, NET and SERT) and its lipid solubility, affecting penetration into the brain. In human cell lines the more lipophilic cathinones, which include the pyrrolidino-cathinones, have been found to cause damage to cells from vascular, respiratory and central nervous systems, which provides a mechanism of toxicity potentially relevant to many synthetic cathinones (Matsunaga and others, 2017).

b) The dose used, which can vary from milligram to gram amounts depending on the specific synthetic cathinone used and the route of administration. If an individual unwittingly consumes a high-potency synthetic cathinone, such as MDPHP, the potential for overdose and associated harm is significant. While this may suggest that lower potency synthetic cathinones would be safer, some may have a narrower window between psychostimulant action and toxic effects so when users increase their dose to achieve desired effects, they also quickly reach harmful doses (Wojcieszak and others, 2018).

c) The route of administration may affect the amount of drug reaching the site of action and the speed at which this happens. Intravenous use, for example, is likely to result in more rapid and greater brain concentrations of synthetic cathinone than the same dose taken orally.

6.6. While the pharmacology is complex, some understanding of how structure affects activity is emerging. Small groups (H or CH_3) on the nitrogen and small (CH_3) side chains favour monoamine releasing activity, while bulkier groups on the amine and longer side chains tend to favour reuptake inhibition. Substituents on the aromatic ring appear to influence selectivity between the monoamine systems (Glennon and Dukat, 2017). As a result, the potency and profile of synthetic cathinones at the monoamine transporters varies

considerably between compounds. This is discussed further for specific cathinones of interest later in this report.

6.7. Several studies suggest that a low SERT:DAT ratio is correlated with liability for dependency (Negus and Banks, 2017). Compounds with distinct DAT-blocking properties tend to be addictive, while those with distinct SERT-blocking properties tend to be empathogens/entactogens, with lower misuse liability. One study suggests a greater than 10-fold differences in transporter selectivity is needed to see these distinct effects (Rudin and others, 2021). This, however, is probably an oversimplification. One of the most addictive compounds is cocaine, but this has a SERT:DAT ratio of only 1.87. Methylphenidate, however, has a very high SERT:DAT ratio (greater than 1000) (Han and Gu, 2006), but a lower addictive potential (Kollins, 2003). Thus, a low SERT:DAT ratio may be a useful indicator of addiction liability, but there are exceptions to the rule and currently there is no evidence for this being the case for synthetic cathinones specifically. Therefore, the SERT:DAT ratio cannot currently be used in isolation as a reliable proxy for the addictive liability in synthetic cathinones and further research is needed. Further detail on the potency of selected synthetic cathinones for NET, DAT and SERT is provided later in this report.

6.8. It has long been suggested that amphetamines, which are structurally similar to synthetic cathinones, are neurotoxic, specifically to the dopamine system through necrosis, oxidative stress and/or mitochondrial dysfunction. These actions are brought about by so-called reverse transport, whereby intracellular concentrations of dopamine are increased by amphetamines acting as substrates at both the DAT and the VMAT2 (Davidson and others, 2001). This leads to a potentially pathological increase in intracellular dopamine. Dopamine is easily oxidised, which can then produce further reactive oxygen and nitrogen species that are toxic to the cells (Davidson and others, 2001). Amphetamines also have multiple mechanisms whereby they are toxic to mitochondria, disturbing cellular energy production and leading to cell death (Barbosa and others, 2015). These mechanisms are still considered the most salient for stimulant neurotoxicity (Rudin and others, 2021). Dopamine neurotoxicity is therefore associated with dopamine releasers or DAT ‘substrates’ rather than DAT blockers. The synthetic cathinone DAT ‘substrate’-like compounds may have similar actions.

6.9. Although numerous rodent studies have demonstrated dopamine neurotoxicity, relevance to human use has been uncertain. It was not until amphetamine users got older that a 3-fold greater incidence of developing Parkinson’s disease (a disease characterised by a loss of dopamine neurons) was demonstrated, confirmed by a recent meta-analysis (Tripathi and others, 2018).

6.10. Other compounds such as MDMA have also been considered to be neurotoxic, specifically to the serotonin (5-hydroxytryptamine, 5-HT) system (Mustafa and others, 2929), although the evidence here is relatively poor.

6.11. Given the structural similarity of many synthetic cathinones to amphetamines, several studies have examined if any are neurotoxic. Butylone, methylone,

pentylone and MDPV all caused neurotoxicity at low micromolar concentrations in human neuroblastoma cells (Valente and others, 2017a; Leong and others, 2020). Other cathinones have been found to be neurotoxic including 4-chloromethcathinone (4-CMC) and N-ethylhexedrone, but at much higher concentrations (100 µM or higher).

6.12. Very high concentrations (low millimolar (mM) range) of the cathinones mephedrone, methylone, MDPV, 4-CMC and various methcathinones have been shown to impair mitochondrial respiration in human neuroblastoma cells (Valente and others, 2017b; Leong and others, 2020; Zhou and others, 2020), although the relevance of these concentrations to those likely to be present during human use is uncertain. Concentrations of the cathinones 3-MMC, 4-MEC, 4-MMC, methylone, pentedrone and MDPV of up to 1 mM had no effect on Human Embryonic Kidney 293 (HEK293) cell viability (Zwartsen and others, 2020).

6.13. In vivo studies found that high doses of mephedrone (40 mg/kg 4 times daily) and MDPV (30 mg/kg 4 times daily) are not particularly neurotoxic in mice (Anneken and others, 2015).

6.14. Jitca and others (2021) reviewed the literature on psychoactive substances and oxidative stress in the dopamine system. No synthetic cathinones were found to have a greater effect on reverse transport than amphetamine or methamphetamine, except for MDPV which caused dopamine efflux with an IC_{50} of 2.3 µM (cf. amphetamine IC_{50} ~4 µM, methamphetamine IC_{50} ~3 µM, mephedrone IC_{50} ~ 30 µM). By contrast, the IC_{50} values for α-PVP, methylone and butylone were all over 100 µM). However, it should be noted that others have not found MDPV to have any significant activity in this regard (Eshleman and others, 2013; Rickli and others, 2015).

6.15. There is some evidence that cathinone neurotoxicity is associated with increasing chain length of the acyl moiety and/or with methyl substituents on the aryl moiety (Gaspar and others, 2018; Morikawa and others, 2021).

6.16. Compounds that cause large increases in synaptic serotonin can evoke serotonin syndrome, characterised by potentially lethal hyperthermia and hypertonicity as well as anxiety, hypertension, tachycardia, delirium and several other symptoms. Overdose of the medicinally licensed cathinone antidepressant bupropion leads to serotonin syndrome in about one in three cases (Sidlak and others, 2020). This sets a precedent for cathinone-evoked serotonin syndrome and a case study with MDPV supports this (Mugele and others, 2012).

6.17. Taken together, there is some evidence for synthetic cathinone-evoked neurotoxicity, but there is no compelling evidence that cathinones are more neurotoxic than amphetamine or methamphetamine, and there is also little or no pre-clinical evidence for neurotoxicity for the newer examples. Further research on neurotoxicity is needed and, in particular, studying any synthetic cathinone with potent amphetamine-like action causing reverse transport of dopamine.

6.18. Many synthetic cathinones increase levels of noradrenaline and serotonin through NET and SERT reuptake inhibition, not just in the brain but also in the periphery. These actions could affect organs other than the brain, including the cardiovascular system. Increased levels of noradrenaline can cause increased heart rate, palpitations and increased blood pressure. Serotonin tends to cause vasoconstriction (Watts and others, 2012), but can also cause heart valve problems through the activation of serotonin 5-HT_{2B} receptors (Elangbam, 2010). MDMA and fenfluramine can cause heart valve problems through increasing serotonin levels and activation of 5-HT_{2B} receptors (Droogmans and others, 2007; Rouaud and others, 2024). Some synthetic cathinones can cause serotonin release (see Table 4), although none are particularly potent. Serotonin release (as opposed to SERT inhibition) is the likely mechanism underlying the increased serotonin causing heart valve problems.

Table 4. Effect of selected compounds, including some synthetic cathinones, on ability to cause neurotransmitter release

Compound	Serotonin release	Norepinephrine release	Dopamine release
Comparator examples			
MDMA[1]	57	77	376
Fenfluramine[1]	79	739	Inactive
Synthetic cathinones			
Mephedrone[2]	5,400	400	1,570
Mexedrone[2]	2,610	6,100	Inactive
4-CEC[2]	780	Inactive	Inactive
Methylone[3]	500	270	220
Eutylone[3]	1020	Inactive	Inactive
Pentylone[3]	650	Inactive	Inactive

Notes:

Data show EC_{50} values (nM)
[1] Rothmann and others, 2001
[2] Eshleman and others, 2019
[3] Glatfelter and others, 2022

6.19. The metabolism of several synthetic cathinones is well characterised and can be broadly grouped according to the structural type of cathinone. The cathinones related to mephedrone are usually subject to *N*-dealkylation (mainly by CYP2D6) and reduction of the carbonyl to hydroxyl. Those with a 3,4-methylenedioxy group undergo less reduction to the hydroxyl but often see demethylenation of the 3,4-methylenedioxy group to the dihydroxy metabolite with further methylation and conjugation. The pyrrolidino-cathinones, however, having the nitrogen as part of the pyrrolidine ring, see reduction to the hydroxyl with many undergoing oxidation of the pyrrolidine ring and/or oxidation of the terminal carbon of the side chain (Majchrzak and others, 2018; Gonçalves and others, 2019). A proportion is also excreted

unchanged. In each case where reduction of the carbonyl to hydroxyl is seen, this gives structures related to ephedrine. The reduction to a hydroxyl introduces an extra stereogenic centre to these molecules, resulting in the formation of diastereomers potentially with different pharmacological properties.

6.20. Unsurprisingly, detailed pharmacokinetic assessment is limited to a few synthetic cathinones and indicates a wide range of bioavailability across the series. The available data are consistent with the rapid onset and short duration of effects reported by users. Several reports indicate that synthetic cathinones freely cross the blood–brain barrier, with MDPV and mephedrone reportedly having particularly high membrane permeability compared to other synthetic cathinones and to amphetamine, methamphetamine and MDMA (Soares and others, 2021).

6.21. Details of the pharmacology of specific cathinones of current concern are provided later in this report.

7 Misuse

7.1. Methods for the synthesis of cathinones were first described in the 1920s and several were licensed as medicines in various countries, although misuse of synthetic cathinones was rare during the 20th century. Methcathinone was first synthesised in 1928 and subsequently used as an antidepressant in the former Soviet Union in the 1930s and 1940s; misuse of this compound was reported in the USSR in the 1970s and in the USA in the 1990s (Gonçalves and others, 2019; Soares and others, 2021). Pyrovalerone was licensed to treat chronic fatigue and as an appetite suppressant in the 1960s, but was subsequently withdrawn and scheduled as a controlled substance after reports of intravenous use (Deniker and others, 1975). Methylone was first synthesised in 1996 as a potential treatment for depression and Parkinson's disease, yet was never licensed as a medicine due to its psychostimulant effects (Soares and others, 2021).

7.2. Recreational use of synthetic cathinones became a more widespread public health issue in the early 2000s, with the emergence of the so-called ‘first-generation’ synthetic cathinones, especially methylone (2005), mephedrone (2007) and MDPV (2009). While some synthetic cathinones that had formerly been used as medicines were already controlled in the UK and internationally (see Section 2, Legitimate use), these particular compounds were not and were part of a larger group of NPS commonly referred to as ‘legal highs’.

7.3. Uncontrolled first-generation synthetic cathinones rapidly became widely available for purchase from open retail sources, including 'head shops', as well as via the internet, with mephedrone dominating the market in the UK. They were commonly referred to as ‘bath salts’, ‘plant food’, or ‘research chemicals’. Contributing to their popularity were their widespread availability, the lack of screening tests for detection, low cost and legal status. Also possibly contributing to their uptake was the lack of availability or low purity of cocaine and MDMA in recreational drug markets at that time (ACMD, 2010;

Schifano and others, 2011; Prosser and Nelson, 2012; Miotto and others, 2013).

7.4. This rapidly expanding use of ‘first-generation’ cathinones was associated with a sharp increase in adverse health effects. For example, in the UK a rapid increase in cases of mephedrone toxicity discussed with UK poisons centres was observed (James and others, 2011) and several deaths implicating mephedrone were reported (ACMD, 2010). Such adverse health effects prompted legal control of these compounds in many countries, including the generic control of synthetic cathinones in the UK, enacted via the MDA in 2010.

7.5. Following control of specific 'first-generation' synthetic cathinones in many countries, further generations of compounds were encountered that evaded many international control measures, with large numbers of different compounds involved, often synthesised in China and South East Asia (Valente and others, 2014). By the end of 2021, the EMCDDA was monitoring 162 different synthetic cathinones, making this the second largest category of NPS in terms of compound numbers after synthetic cannabinoids. Numbers of new compounds reported annually in the EU peaked in 2014 and have subsequently declined (Soares and others, 2021). Sales of synthetic cathinones by open retail sources declined sharply after legal controls were enacted, so users obtained them from the internet and increasingly the dark web, as well as from street dealers.

7.6. Use of mephedrone has declined in the UK over the last decade. The annual number of mephedrone seizures made by law enforcement agencies in England and Wales peaked in the year ending March 2013 and subsequently fell, with reductions in mephedrone seizures also reported from other devolved administrations over a similar time course (Corkery and others, 2018). There have also been reductions in reported mephedrone use, while death registrations have reduced since 2015 (see Section 4, Current UK prevalence).

7.7. Following international control measures for mephedrone and other first-generation synthetic cathinones, examples of 'second generation' compounds began to appear, including naphyrone, butylone, pentylone, 4-methyl-N-ethylcathinone (4-MEC), 4-fluoromethcathinone, 4-methyl-α-pyrrolidinopropiophenone (4-MePPP) and 3,4-methylenedioxy-α-pyrrolidinobutiophenone (MDPBP) (Gonçalves and others, 2019).

7.8. Subsequently a ‘third generation’ of compounds appeared, initially 3,4-dimethylmethcathinone (3,4-DMMC), then subsequently pentedrone (α-methylaminovalerophenone) and α-pyrrolidinopentiophenone (α-PVP) (Valente and others, 2014). The latter, marketed as ‘flakka’ or ‘gravel’, became popular in the USA and Europe between 2011 and 2015 (Crespi 2016; Castellanos and others, 2018; Soares and others, 2021). The similar compounds α-PiHP and α-PHP were first detected around 2016 (Kuropka and others, 2023a).

7.9. More recent data from drug seizures made in EU member states indicate that 3-CMC was the most common synthetic cathinone in 2021, with 3-MMC, 4-CMC and N-ethyhexedrone also found in appreciable quantities (EMCDDA, 2023; Nadal-Gratacós and others, 2024). While these second and third generation synthetic cathinones evaded some international legislation involving control of compounds by name, they were controlled in the UK through the generic approach that was used.

Desired effects

7.10. The effects that users seek from these compounds include enhancements in energy, alertness, mood, sociability, sensory experiences, empathy, confidence, sexual arousal/libido and wellbeing (Watterson and others, 2014). Users, however, can also experience anxiety, paranoia and diminished appetite (Drug Policy Alliance, 2016).

7.11. People using mephedrone reported appreciation for the 'high', enhanced confidence, and elated feelings that seemingly suppressed problems (Brookman and others, 2017). These effects make synthetic cathinones attractive within the night-time economy as ‘party’ drugs.

User profiles

7.12. The transition from legal highs to controlled drugs after 2010 in the UK and elsewhere has affected the profiles of users. Prior to control, users of ‘legal high’ synthetic cathinones were often younger males who used the synthetic cathinones alone or with alcohol (James and others, 2011). There was international concern via the Drug Enforcement Administration (DEA) that the street names for synthetic cathinones might glamourise these substances, especially for younger people (Karila and others, 2015). In 2010, about one fifth of young people (14- to 20-year-olds) in a sample group reported using mephedrone (Karila and others, 2015).

7.13. Subsequently, while those using synthetic cathinones continued to be younger males aged 18 to 35 years, including ‘psychonauts’, ‘clubbers’ or festival attendees, they were increasingly polydrug users, including high-risk intravenous users (EMCDDA, 2015; Benschop and others, 2017). In reported 2010 to 2015 data, recent cathinone use was found to be associated with daily tobacco and polydrug use. Among poly-NPS users, in decreasing order of prevalence, recent cathinone use was associated with the intake of phenethylamines, tryptamines, synthetic cannabinoid receptor agonists (SCRAs), plants and extracts, arylcyclohexamines, piperazines and aminoindanes (Sutherland and others, 2016). Injecting cathinone users were often primary injectors of other drugs, who switched to or added cathinones to their repertoire. Some had been opioid abstinent for extended periods before injecting cathinones.

7.14. A recent survey in Germany indicated that synthetic cathinone users were usually unmarried, unemployed and with little education (Schmoll and others, 2018; Manke and others, 2022). Data from the NPSUM in the UK for the

period 2019 to 2023 provided for this report demonstrates that a high proportion of drug-related deaths in the UK involving a synthetic cathinone were male, aged 25 to 54 and in the lowest deciles of deprivation index according to postcode, or of no fixed abode.

7.15. Prevalence of synthetic cathinone use has been high in men who have sex with men, including in the context of chemsex, when mephedrone may be used in combination with other drugs including methamphetamine and/or GHB (Giorgetti and others, 2017). Intravenous use of cathinones may also occur in this context (Dargan and others, 2010; Pieprzyca and others, 2020). Behaviour associated with chemsex including multiple partners, condomless sex or anal or penile trauma may increase the risk of sexually transmitted diseases, including hepatitis C and human immunodeficiency virus (HIV) infections (Karila and others, 2015).

Modes of use

7.16. Synthetic cathinones are usually sold as powders or crystals, but capsules and tablets can also be encountered, as well as vapes containing cathinone. Products may not contain the compounds advertised and purchasers are often unaware of the precise substances they are using. Products may contain combinations of synthetic cathinones or combinations of cathinones with other substances, such as MDMA, meta-chlorophenylpiperazine (mCPP) or caffeine (Zawilska and others, 2013; German and others, 2014; Guirguis and others, 2017). Synthetic cathinones may also be found in tablets sold as other drugs, such as MDMA. For example, the English Festival Survey reported that MDMA was detected in 93% samples resembling ecstasy tablets in 2019 but only 55% in 2021, while synthetic cathinones were detected in 0.2% of these samples in 2019 and 19.4% in 2021. This suggests increasing substitution of synthetic cathinones for MDMA in these products over that time. The most common synthetic cathinones detected in this series were 4-CMC, 3-methylmethcathinone (3-MMC) and eutylone (Pascoe and others, 2022).

7.17. Synthetic cathinones are commonly used by nasal insufflation (snorted, such as from a key – ‘keying’) or ingested orally (wrapped in cigarette paper – ‘bombing’, or swallowed as tablets or capsules). Due to their water solubility, they can also be dissolved in water and injected intramuscularly (IM) or intravenously (IV – ‘slamming’), sometimes with heroin and especially by high-risk drug users, as described above (Dargan and others, 2010). Rectal, gingival (gum), sublingual (under the tongue) and ocular application (application to the cornea of the eye – ‘eyeballing’) have also been described, as well as inhalation using ‘vapes’ (Soares and others, 2021). Smoking of some products has also been reported, sometimes in pipes, including smoking of so-called ‘monkey dust’. Of note, while earlier seizures of MDPHP were of the hydrochloride salt, more recent seizures were commonly of the base form, which is more suitable for smoking. It is also common for multiple routes to be used in a single session (Gonçalves and others, 2019). Development of tolerance may encourage dose increases.

7.18. Use commonly occurs with other drugs, including amphetamines, cocaine, GHB/GBL, cannabinoids, ketamine and/or alcohol, or prescription drugs, including benzodiazepines and Z-drugs (Soares and others, 2021). In an American survey of synthetic cathinone users, most used these compounds at least once a month, usually with other people, in the evening or at night and in combination with other substances such as cannabis and alcohol. Reported reasons for using synthetic cathinones included its stimulating effects, curiosity, substitution for another drug, and being at a party/music event. (Ashrafioun and others, 2016).

7.19. The doses of synthetic cathinones used vary widely depending on the potency and bioavailability of the compound involved and the route of administration. Doses are typically lower for more potent compounds such as MDPV compared with mephedrone, and higher for oral ingestion than nasal insufflation. For mephedrone, higher oral doses are needed when it is swallowed compared with nasal use because of first-pass metabolism (metabolism of ingested and absorbed drug by the liver before it reaches the systemic bloodstream) (Martínez-Clemente and others, 2013). Nasal insufflation of mephedrone, however, is associated with painful irritant effects on the nasal mucosa. Synthetic cathinone doses may increase with duration of use and may be substantial during binge sessions (Soares and others, 2021).

8 Dependency, treatment and recovery

8.1. Synthetic cathinones are powerful stimulant psychoactive drugs that impact the brain's reward system, and their sustained use can precipitate compulsive drug-seeking behaviours with a high probability of dependence and an increase in the possibility of a drug-related death (Prosser and Nelson, 2012; Chen and others, 2024).

8.2. Poyatos and others reviewed the 'abuse potential' of several synthetic cathinones. In general, cathinone, diethylpropion, mephedrone and methylone showed similar stimulant profiles to MDMA and amphetamine. All precipitate stimulant-like effects, intensify euphoria and increase sociability and wellbeing (Poyatos and others, 2022a; Poyatos and others, 2022b). A double-blind randomised controlled trial investigating the clinical pharmacology of mephedrone and its relative 'abuse liability' compared with MDMA showed that mephedrone-induced stimulant effects were similar to those of MDMA, but their onset was faster and duration shorter (Papaseit and others, 2016).

8.3. When individuals experience what they perceive as greater 'positive' effects of cathinones, there is a greater likelihood of increased use, leading to harmful use and dependence (Poyatos and others, 2022a; Poyatos and others, 2022b; Papaseit and others, 2016).

8.4. Longer-term pharmacological treatments for stimulant use disorders (including those involving synthetic cathinones) have not been approved in the UK or the USA. Results from a systematic review found insufficient evidence for the effectiveness of psychostimulants, *N*-acetylcysteine, opioid agonist therapy,

disulfiram, or antidepressants to support or discount their use (Ronsley and others, 2020). It was recognised that there is a substantial gap in the evidence and that more methodologically rigorous research is needed on the efficacy of pharmacological treatments for stimulant use disorders.

8.5. The same review, however, did support the use of psychosocial interventions in working with problematic cathinone use, which usually manifests as part of a polydrug use trajectory. The literature, which is derived primarily from American sources, highlights contingency management as an evidence-based approach that shows some efficacy when combined with cognitive behavioural therapy (CBT). However, the latter demonstrates less effectiveness as a standalone treatment (Ronsley and others, 2020). Treatment approaches that combine contingency management with CBT or a community reinforcement approach show the greatest effectiveness in clinical studies (Carroll and others, 2021).

9 Health harms

9.1. The acute toxicity associated with the most commonly used synthetic cathinone, mephedrone, has been very widely described in the scientific literature. It was reviewed in the risk assessments undertaken by ACMD and EMCDDA in 2010 (ACMD, 2010; Dargan and others, 2010; EMCDDA, 2011; James and others, 2011; Winstock and others, 2011; Wood and Dargan, 2012a, 2012b; Papaseit and others, 2017).

9.2. These sources of information show that the acute toxic health effects seen with mephedrone are broadly similar to those of other stimulants, such as amphetamine and MDMA, and are also likely to reflect those of many other synthetic cathinones. These effects include:

- local effects: nasal insufflation may be associated with nasal irritation, sore mouth/throat and nose bleeds (Dargan and others, 2011); uvulitis and spontaneous cervical subcutaneous emphysema have rarely been reported (Murphy and Haughey, 2014; Maan and D'Souza, 2012);

- neuropsychiatric features: euphoria, increased alertness, intensified emotions and enhanced self-esteem may occur initially, but adverse effects include agitation, anxiety, confusion, tremor, headaches, hallucinations and delusions, seizures and post-use depression;

- cardiovascular features such as palpitations, tachycardia, chest pain or hypertension;

- other features such as nausea and vomiting, loss of appetite, dilated pupils, blurred vision, hyperthermia and rhabdomyolysis.

9.3. Reported complications include stroke, myocardial infarction, marked hyponatraemia, disseminated intravascular coagulation, pulmonary oedema, hepatic and/or renal failure, ventricular tachycardia or ventricular fibrillation

(James and others, 2011; Wood and Dargan, 2012a, 2012b; Di Candia and others, 2022; UNODC, 2024).

9.4. Cathinone-related fatalities are often attributed to hyperthermia, hypertension, cardiac arrest and serotonin syndrome (UNODC, 2024).

9.5. Suicidality may also be associated with synthetic cathinone use (Schifano and others, 2020) and when used with synthetic cannabinoids and prescription medication (Klavž and others, 2016).

9.6. Management of acute toxicity caused by synthetic cathinones is generally supportive and targeted at the observed clinical features. There is no specific antidote for cathinone toxicity and often no specific therapy is needed. In more severe cases, agitation, behavioural disturbances, tachycardia, hypertension, hyperthermia and seizures may all be improved by administration of a benzodiazepine, such as diazepam. Occasionally, high benzodiazepine doses are needed to control severe agitation and alternative drugs, such as haloperidol or ketamine, are sometimes required. Serotonin syndrome can be managed using a benzodiazepine or a serotonin (5-HT) antagonist, such as cyproheptadine or chlorpromazine. Hyperthermia may require active cooling methods, including external or internal cooling measures.

10 Social harms

10.1. Little published evidence on the societal impacts from use of synthetic cathinones has been identified for this review, despite their use for more than a decade. Social harms related to the use of synthetic cathinones are likely to reflect those associated with other psychostimulants and drug use more broadly. Some users can integrate the use of psychostimulants into their lives without adverse consequences, while others (and especially heavy users) may face adverse social or financial consequences (Rosenkranz and others, 2023). It is also important to note that polydrug use is common in this context and social harms may result from other substances consumed. Synthetic cathinone use has become increasingly associated with social deprivation and homelessness over the last decade (McCormack and others, 2023a), although there is also significant use by groups who are less likely to be impacted adversely. These include younger people, including those attending festivals, as well as men who have sex with men, who may use synthetic cathinones such as mephedrone in the context of chemsex, often with other substances (Giorgetti and others, 2017). The social harms associated with using synthetic cathinones are likely to be influenced by these different contexts of use.

10.2. All psychostimulants, including synthetic cathinones, can aggravate antisocial behaviour including aggressive or disruptive behaviour, sometimes exacerbated by paranoia or hallucinations, although not all synthetic cathinone users behave in antisocial ways (McCormack and others, 2023a; McCormack and others, 2023b). Some individuals or groups of users may cause local disruption, creating anxiety in local populations and requiring a response from the police and the NHS. This can consume significant amounts

of police and healthcare resources in areas where the prevalence of this type of drug use is high. For NPS more generally, police staff perceive NPS users as volatile in custody and feel less knowledgeable about how to respond to the needs of affected detainees, compared to those affected by alcohol or heroin (Addison and others, 2017).

10.3. There are also costs to longer-term drug treatment and recovery, although it is relatively uncommon for synthetic cathinones to be the primary substance needing treatment in those using these services.

10.4. The costs of purchasing synthetic cathinones are generally not high and, as a result, their use does not appear to have a major impact on acquisitive crimes, such as theft. However, violent behaviour may occur after use and there is some evidence that this may include sexual violence (Page and Temple-Malt, 2018).

10.5. Family life can be negatively affected by synthetic cathinone use, as evidenced by research examining users of mephedrone (Brookman and others, 2017) or NPS more broadly (Page and Temple-Malt, 2018). This may result in family breakdown and, in some cases, homelessness.

10.6. While homelessness may be a consequence of drug use, structural factors such as homelessness or social deprivation may also encourage drug use (Addison, 2023). Those who are homeless may use synthetic cathinones as a distraction from the circumstances of their lives or to remain vigilant about the threats they may face living on the streets. Affected individuals may become vulnerable to crime, including trafficking and sexual exploitation. Further evidence of how this has affected users in and around North Staffordshire is described later in this report and ACMD has previously advised on drug-related harms in homeless populations and how they can be reduced (ACMD, 2019).

10.7. There may be significant impacts on an individual from a criminal conviction related to the MDA; for example, for possession or supply of a controlled drug such as a synthetic cathinone. Besides criminal penalties, a conviction may have substantial detrimental effects on prospects for education, employment and housing. Risks to education or employment from a criminal conviction are particularly important for students and employees, but for homeless polydrug users who are unlikely to be in education or employment, loss of access to housing is likely to be more important.

10.8. There may be a substantial stigma associated with synthetic cathinone use, especially within homeless or other socially deprived groups, and this may be an important barrier to their access to services (McCormack and others, 2023b). There may be less stigma associated with synthetic cathinone use in other circumstances, such as at festivals or in clubs.

10.9. Further details on the individual and societal impacts of synthetic cathinone use and specifically the product referred to as ‘monkey dust’ used in Staffordshire and surrounding areas are provided later in this report.

11 Current issues of concern

11.1 Following a review of the compounds detected in the UK over the last 5 years, the working group concentrated on 3 specific themes related to synthetic cathinones as follows:

(i) Cathinone use in North Staffordshire and its environs. This issue was specifically referred to in the ministerial commissioning letter for this report.

(ii) Synthetic cathinones currently most commonly associated with drug-related deaths in the UK. It is appropriate to consider these compounds and advise on appropriate measures to reduce their public health impact. It is important to note that there is substantial overlap between this group and the compounds detected in and around North Staffordshire. The specific compounds considered are described in Sections 12 and 13.

(iii) Currently uncontrolled synthetic cathinones that have been detected in the UK or in Europe. It is important to consider whether all or some of these compounds present sufficient actual or potential risk of harms in the UK to merit control under the MDA 1971. The specific compounds considered are described in Section 13.

12 Cathinone use in North Staffordshire and its environs

12.1. In order to obtain further evidence about the impact of synthetic cathinone use in North Staffordshire and its environs, ACMD attended and engaged with a range of local stakeholders in 2023. These included several local charities and organisations, academia and Staffordshire Police. In addition to the oral evidence collected in 2023, ACMD welcomed written submissions on synthetic cathinone use from various individuals and organisations throughout the UK via a public Call for Evidence in 2024. The use of synthetic cathinones has emerged as a problem in Staffordshire, Shropshire and Cheshire in recent years, with markets reported to be concentrated in Stoke-on-Trent, Telford, Shrewsbury, Newcastle under Lyme, Stone, Stafford and Uttoxeter. They are commonly sold as a product referred to as ‘monkey dust’, which first came to public attention in 2013 (Atkinson and Sumnall, 2020) and may contain one of several different synthetic cathinone compounds (see below). The use of ‘monkey dust’ has become an issue of concern for law enforcement and wider public services due to its impact on users and communities.

User characteristics

12.2. Users are often from deprived communities and include people who are socially excluded and vulnerable, as well as prison leavers. Many of the smaller group of drug users who use synthetic cathinones are reported by stakeholders to be polydrug users with current or previous use of crack cocaine or heroin. Many live in temporary housing, such as hostels, or are homeless.

12.3. ‘Monkey dust’ may be taken over short (a few days) or much longer periods of time and may be used alone or with other substances. Users may source it from local street dealers or purchase it directly via the internet (McCormack and others, 2023b). Local stakeholder responses also suggested sourcing of ‘monkey dust’ components from the dark web, with distribution and supply involving organised crime groups.

12.4. ‘Monkey dust’ is generally taken by smoking, often using a pipe, although other routes may be used, including intravenous administration (McCormack and others, 2023a).

12.5. Local stakeholders report that consumption frequently occurs in public areas in the community or derelict buildings, and these may also be sites of drug dealing (McCormack and others, 2023b).

Drivers for use

12.6. An important driver for the use of ‘monkey dust’ is the cost compared to other drugs of choice. It has been approximately 2 to 3 times cheaper than the equivalent weight of crack or powder cocaine and is reported to have longer lasting psychostimulant effects than other stimulants, including cocaine and amphetamines (McCormack and others, 2023b). Prices are reported to range from approximately £15 to £40 per gram, with street deals available for amounts as small as 0.1 to 0.2g (£1.50 to £8). Prices, however, fluctuate daily and have recently been similar to those of heroin due to local supply shortages, leading to the cutting of ‘monkey dust’ with heroin and other drugs such as sildenafil (Viagra®), paracetamol and caffeine.

12.7. People who have reported using ‘monkey dust’ have indicated that they take the drug as self-medication for their mental health and as a ‘coping mechanism’ for past or current abuses (McCormack and others, 2023b). International research highlights that homeless people are particularly vulnerable to becoming victims of crime, including violent attacks (Larney and others, 2009; Sadiki and Steyn, 2021) and there is also evidence of this in the UK (Long, 2024). As such, a homeless person may use cheap synthetic stimulants to stay alert to reduce the likelihood of becoming a victim of crime.

12.8. Users reported using ‘monkey dust’ to increase libido and feelings of sexual confidence. Sexual violence has been noted by Page and Temple-Malt (2018), and was also reported by stakeholders.

Compounds included

12.9. There is limited information about the specific compounds included in ‘monkey dust’ products. Manchester Drug Analysis and Knowledge Exchange (MANDRAKE) analysed 21 samples of ‘monkey dust’ powders provided by Staffordshire Police in October 2018. All were confirmed to contain MDPHP, with calculated purity ranging from 34% to 100%.

12.10. More recently, Staffordshire University analysed 30 individual powder samples seized by Staffordshire Police between February 2022 and September 2023,

together with 7 samples seized by West Mercia Police between January and November 2023. Of these 37 samples:

- 26 contained MDPHP, with purity ranging from 31% to 90% (median 55%); caffeine was also detected in 12 samples
- 2 contained α-PiHP, with purities of 57% and 69%; one of these also contained caffeine
- 1 contained α-PHP with no other substance detected; the purity was not estimated due to a lack of a certified reference standard

12.11. Other substances detected included cocaine (2 samples), diacetylmorphine (heroin – 2 samples) and ketamine (1 sample). No active drug was detected in 3 samples.

12.12. These limited data demonstrate that most samples of 'monkey dust' contain pyrrolidino-cathinones, especially MDPHP, but occasionally α-PiHP or α-PHP. Caffeine may also be included in some preparations, while a few contain non-cathinone-controlled drugs or no active substance at all. Stakeholders have reported other substances cut with 'monkey dust' including sildenafil (Viagra®), although no direct analytical evidence of this has been provided.

12.13. It is important to recognise that there has been limited testing of substances sold as 'monkey dust' and there remains the possibility that other substances are in circulation but have been detected less often due to a lower propensity for linked problems. Without more detailed monitoring, it is not possible to ascertain if compounds that are more potent by weight are being diluted with excipients, or know the purity of preparations being sold.

12.14. There is useful information available about the synthetic cathinones associated with drug-related deaths in Staffordshire from NPSUM. Of all the deaths reported from across the UK, 14 of the 15 involving MDPHP, all 28 of the α-PHP deaths and 4 of the 7 α-PVP deaths were reported from Staffordshire and most are likely to be associated with use of 'monkey dust'. Of 75 deaths involving a synthetic cathinone recorded between 2019 and 2023 from across the UK, 52% occurred in Staffordshire and pyrrolidino-cathinones were involved in 14.5% of all drug-related deaths from that area. These data emphasise how the severe health impacts of pyrrolidino-cathinones are localised in Staffordshire and occur relatively infrequently elsewhere in the UK.

12.15. Further emphasising the local nature of the problem, MDPHP detections in seized drug samples from across the UK and analysed by Eurofins mainly involved samples seized by police forces in the West Midlands, Staffordshire and West Mercia, with most from Staffordshire; a large proportion of these seizures were made during 2023 (Annex C). MDPHP has also been detected elsewhere, for example in Greater Manchester (MANDRAKE) and Blackpool (IONA), but this appears much less common.

12.16. The NPSUM data demonstrates that across the UK, compared with those involving mephedrone, drug-related deaths involving MDPHP, α-PVP and α-PiHP (of which the great majority are reported from Staffordshire and likely

to be ‘monkey dust’ related) more commonly involved people over 45 years of age, known drug users, and those in the lowest deciles of social deprivation and (at least for MDPHP) of no fixed abode. Although females are less often involved than males in both groups, the proportion of females was higher in the group where MDPHP, α-PVP or α-PiHP were detected compared to those where mephedrone was detected (see NPSUM in Annex C).

12.17. Seizures of ‘monkey dust’ in Staffordshire decreased in 2023 (40 seizures) compared to 2022 (65 seizures); however, the actual quantity of drug recovered increased nearly 7-fold (from 1,342g to 9,162g). This may be attributable to success from intensified local policing activity in taking on dealers.

Impacts on users

12.18. Use of the psychoactive substances found in ‘monkey dust’ has a significant detrimental impact on users, with some exhibiting effects including severe behavioural disturbances often associated with noise and erratic, unpredictable and antisocial behaviour.

12.19. Professionals in North Staffordshire and environs who work with people who use ‘monkey dust’ report that effects can include paranoia and hallucinations; for example, people believing that creatures were in their veins and self-harming to try to remove them (McCormack and others, 2023b). Police stakeholder evidence highlights that they frequently deal with individuals believed to be under the effects of ‘monkey dust’ in incidents that include rooftop sieges and affected individuals jumping from rooftops, running in front of moving traffic or stripping naked in busy town centres. It is important to note, however, that drug testing is rare in response to these incidents, so there remains uncertainty about which specific compounds (cathinone or non-cathinone) are involved. Many of those involved have pre-existing mental health conditions and trauma from adverse experiences, and these may considerably contribute to their behaviour.

12.20. ED staff also report ‘monkey dust’ users displaying unpredictable and/or risk-taking behaviour, and of being at high risk of causing physical harm to themselves or others. Severe and prolonged agitation or drug-induced psychosis may occur, requiring restraint by several staff. This sometimes requires rapid tranquilisation with intramuscular sedatives as the least restrictive and safest option. The doses required may be much higher than for other similar presentations (for example, cocaine-induced psychosis) and repeat dosing may be necessary, including emergency anaesthesia and transfer to intensive care in extreme circumstances. The management of those under the influence of ‘monkey dust’ can impact on the safe management of other patients, given the noise and disruption often involved and the disproportionate use of staff and equipment.

12.21. Reduced responsiveness, increased calmness and stupefaction have also been described following ‘monkey dust’ use. These are not anticipated effects of synthetic cathinones, although other substances being used may contribute

to all clinical effects observed, as those using ‘monkey dust’ are commonly multi-drug users (McCormack and others, 2023b).

12.22. Impacts on skin, teeth and hair were reported by users, and burns associated with smoking and wound infections, chronic leg ulcers and deep venous thrombosis after intravenous use. Local stakeholders also suggested lung damage, similar to ‘crack lung’, from inhaling ‘monkey dust’ with other substances. Healthcare staff report longer-term adverse effects, with users displaying mental health problems that are precipitated or exacerbated by using ‘monkey dust’.

12.23. Users describe ‘monkey dust’ as “morish”, “mentally addictive” or an “obsession”, but did not describe physical addiction or withdrawal symptoms. Use is associated with a disorganised lifestyle, including poor personal hygiene, not remembering, or attending appointments and not picking up prescriptions (McCormack and others, 2023a; McCormack and others, 2023b).

12.24. 'Monkey dust' users are often excluded from services, including GPs, mental health and housing/accommodation services, which can have a negative impact on their recovery (McCormack and others, 2023b). This is largely due to the perceived risks around paranoia and erratic behaviour, risk of property damage, and the potential impact on other people if accommodation is shared. As a result, social issues can become further exacerbated, leading to more severe demands on the time and resources of support services. Exclusion from access to housing services is a particular disadvantage for a population that is often homeless or in temporary accommodation, and this may cause further drug use.

Impact on communities

12.25. When use of ‘monkey dust’ is prevalent within a community, this can have local financial and commercial impacts, with negative public perception and social media representation. This results in reduced public footfall with consequent adverse effects on local businesses, negatively impacting economic and social wellbeing.

12.26. Incidents involving ‘monkey dust’ consumption are often protracted and resource intensive for the police and other public services to resolve. They also cause significant community safety concerns due to perception and impact. They are often highlighted in the local media, generating further stigma and fear. Services more broadly have suggested that responding to people in crisis, who self-report ‘monkey dust’ use and are displaying behaviour that is a safeguarding concern, is resource intensive for police and other services (McCormack and others, 2023b).

12.27. ‘Monkey dust’ is not reported to result in the levels of acquisitive crime associated with some Class A drugs, whereby users have traditionally needed to fund their habit, with one reason being a lower pricing point compared with other drugs. However, stakeholders have associated ‘monkey dust’ use with shoplifting and criminal damage. As well as being vulnerable to violence,

synthetic cathinone users may exhibit violent behaviour towards others, with concerns raised in particular about sexual violence.

12.28. Evidence from Telford has indicated that female sex workers have experienced sexual violence from males alleged to be using ‘monkey dust’. Furthermore, a person engaged in sex work may be coerced to consume the drug for exploitative reasons, and research suggests that homeless women are also vulnerable to exploitative sexual violence associated with ‘monkey dust’ use (Page and Temple-Malt, 2018). Stakeholders also report ‘monkey dust’ being used to pay for sex work.

12.29. The local media has stigmatised ‘monkey dust’ users with links to “violent”, “superhuman” and “zombie” behaviour (Atkinson and Sumnall, 2020). Such media depictions have influenced perceptions in affected communities and have seemingly created barriers in access to support services (McCormack and others, 2023b). Stigma can also be gender specific in that females with children, or who are engaged in sex work, can be among the most stigmatised (Page and others, 2024). Young people in Stoke-on-Trent view NPS drug users in stigmatising ways and although this can have a negative impact on users, the perceived stigma can discourage some younger people from the engaging in NPS use [Page & Temple-Malt, 2018].

12.30. As with other synthetic cathinones and drugs more widely, family life can be negatively affected by ‘monkey dust’ use and this may result in homelessness and increased vulnerability to associated social harms including trafficking and sexual exploitation, which are cited harms in the evidence provided for this review by local organisations in Stoke-on-Trent and Staffordshire.

12.31. Social harms are particularly apparent in vulnerable groups, such as the homeless. According to the NPSUM report, synthetic cathinone drug-related deaths are concentrated amongst those in the lowest deciles of social deprivation indices, including people with no fixed abode and the unemployed.

12.32. Published reports (McCormack and others, 2023a; Page and Temple-Malt, 2018) and the wider Call for Evidence for this review note that ‘monkey dust’ use in Staffordshire is common in those with multiple disadvantages, commonly alongside other harmful substances including other NPSs. It should be noted that these studies were not designed to explore the use of ‘monkey dust’ in the wider population, either locally, where these pieces of work were carried out, or nationally. In the users who were studied, adverse childhood experiences, including abuse or neglect, current mental health concerns and polydrug use were common. Their frequent homelessness inevitably puts this cohort more often in contact with blue light and support services. Drug use on the streets, such as by rough sleepers, is generally more in public view and, as a result, may be recorded more completely than use by the wider public, and also puts these users at increased risk of stigmatisation. Homeless users are also more accessible to researchers through support services.

Challenges for local services

12.33. Responding to incidents involving ‘monkey dust’ users can be resource intensive for the police and other agencies. The police reported that an analysis of recorded incidents demonstrated almost 15 calls per day in Stoke-on-Trent during 2023 to 2024. Given the severity of the effects that use of this drug can produce and the associated crime and antisocial behaviour, it is likely that many of these calls would result in a deployment of a policing resource. Considering the variety in incident characteristics, it is not possible to accurately apportion an average time and hence cost to policing with any degree of confidence. It is common for the same person to be detained on multiple separate occasions for ‘monkey dust’ use.

12.34. The physiological and psychological impact that ‘monkey dust’ causes to its users often translates to operational challenges in managing individuals detained in police custody. Detainees may not be physically fit to be interviewed for significant periods and this creates blockages in time/resourcing to process detainees.

12.35. Criminal prosecution regarding ‘monkey dust’ is made no easier due to the lack of any approved field-testing equipment, meaning that formal forensic submission and examination is required to meet the criminal burden of proof for simple possession offences. This is a time-consuming process, which places further burdens an already stretched criminal justice system. Only opioids, cocaine, MDMA and amphetamines are tested for in custody and probation and those managed in the community are fully aware of this. The absence of approved field testing prevents the issuing of warnings or licence conditions following arrests related to other substances. It also prevents the accurate recording of effect and impact. Development of reliable Home Office field-testing would therefore enable clear identification of the substance resulting in appropriate finalisation including drug treatment and rehabilitation, as well as better targeting of samples to be sent for more detailed forensic analysis.

12.36. The use of intelligence by Staffordshire Police to target suppliers of ‘monkey dust’ has recently had some success in Stoke-on-Trent. Covert tactical options considered for many conventional law enforcement operations are limited regarding ‘monkey dust’ due to the behaviour displayed by users and its physiological effects. These factors render some policing tactical options used in combatting the supply of controlled drugs ineffective and inappropriate.

12.37. Operation Rivent was commissioned in May 2022 to deal with the impact ‘monkey dust’ was having on local communities in Stoke-on-Trent. The Staffordshire Police tactical approach was consistent with the National Drugs Strategy and included disruption and enforcement (targeted enforcement of supply chains at both street level and of upstream producers and distributors) and vulnerability and safeguarding (helping users into treatment and recovery through established partnership pathways). An operational review conducted

on the operational activities between May 2022 and December 2023 highlighted some learning points as follows:

- there were barriers in accessing referral pathways for helping users into support and a lack of treatment and rehabilitation options thereafter;

- disruption and enforcement were effective, with more than 60 arrests made in the first 6 months, and commodity seized (including seizures at the UK border) led to a reduction in available ‘monkey dust’ in the Stoke-on-Trent area; however, this also raised alternative questions regarding the ineffectiveness of screening and detection at the borders given drugs that clearly have entered the country;

- a better understanding is required by the police of ‘monkey dust’ and its effects in users.

12.38. During 2022 and 2023, the Staffordshire University Forensic Science Faculty conducted forensic testing on seized samples of ‘monkey dust’ to improve understanding of this substance (chemical composition, purity, forensic batch comparison, cutting agents used). This ran in parallel with a local partnership working group. Analytical results from this work have already been described (paragraph 12.10).

12.39. Use of ‘monkey dust’ places strains on other services apart from the police. These include ambulance and fire services, hospital EDs, mental health and drug treatment services.

12.40. Users often present with mental health conditions, as cathinones act to exacerbate associated symptoms (such as extreme paranoia, prolonged psychosis). This leads to increasing concern for the welfare and safety of affected individuals.

12.41. Drug and mental health services, both currently under pressure, rarely engage with individuals they perceive to be using ‘monkey dust’ during times of ‘crisis’, such as when displaying distress related to hallucinations. Following a recent evaluation of pathways for people experiencing co-occurring mental health and drug and/or alcohol use in Stoke-on-Trent reported by local stakeholders, conflict was identified between drug treatment providers and mental health providers. This often resulted in individuals being left without healthcare support and the police being the only service that will attend to them. This can also result in opportunities for early intervention being missed, and individuals being left to escalate until they become so disruptive the police are called by members of the public.

12.42. Stakeholders reported a lack of cathinone-related education, training and awareness on short- or long-term health problems affecting users and lack of support for users, other than community drug and alcohol services.

12.43. Users do not perceive traditional community drug and alcohol services as suitable support, regarding these as only appropriate for traditional

substances such as heroin or cocaine. There is a particular difficulty in accessing mental health support alongside substance misuse treatment.

13 Compounds of concern

13.1. This section discusses the pharmacology and health harms of synthetic cathinones that have been recently involved in drug-related deaths in the UK, and/or have been identified in 'monkey dust' products in Staffordshire. It also discusses examples that are not currently covered by the synthetic cathinones generic text in the MDA.

Pyrrolidino-cathinones

13.2. These compounds, including α-PHP, α-PiHP, MDPHP, α-PVP and MDPV, are structurally related to pyrovalerone, possessing a pyrrolidino ring at the nitrogen position of the cathinone structure instead of a primary amine or N-methyl amine, and an extended α-carbon side chain (Zaitsu and others, 2014; Zawilska and Wojcieszak, 2017). This makes them more lipophilic than other cathinones and this may result in them penetrating the brain more easily (Simmler and others, 2013).

13.3. Most pyrrolidino-cathinones have very high potency at both the DAT and NET transporter systems (Table 5) compared to a wide range of other cathinone and non-cathinone stimulants, including cocaine, methamphetamine and methcathinone (WHO, 2022). For comparison, cocaine is about 10 times less potent at NET and DAT than α-PHP, MDPHP and α-PVP. The pyrrolidino-cathinones also show low potency at SERT, and therefore high selectivity for DAT over SERT (low SERT/DAT ratio). They are therefore likely to produce marked central dopaminergic and adrenergic actions, as well as marked 'cocaine-like' peripheral adrenergic stimulation and cardiovascular toxicity. Substantial stimulant effects have been demonstrated in rats from administration of pyrrolidino-cathinones, specifically α-PPP, α-PHP and α-PVP, especially when given intravenously (Taffe and others, 2021). Low potency for SERT suggests that they would have weak or no empathogenic effects.

13.4. Use of MDPV and its methylenedioxy-*N*-pyrrolidine analogues may result in anxiety, paranoia, memory loss and aggression (UNODC, 2024), while MDPV usage was associated with combative and violent behaviour, chest pain and blurred vision in a US study (Spiller and others, 2011).

Table 5. IC_{50} values for inhibition of transporters for selected pyrrolidino-cathinones, compared with mephedrone

Compound	Number of studies	NET (nM)	DAT (nM)	SERT (nM)	SERT/DAT	Refs
Pyrrolidino-cathinones						
α-PiHP	1	150	13.4	50,000	3,730	[1]
α-PVP	7	37.4	32	117,600	3,675	[1-7]
α-PHP	2	43	35.7	127,500	3,571	[2,4]
α-PPP	3	466	264	180,000	682	[2,4,5]
MDPV	6	29	25.7	6,373	248	[2-5,8,9]
Pyrovalerone	3	46	57	12,900	226	[2-5,10]
MDPHP	1	60	50	9,000	180	[2]
α-PBP	1	91.5	63	10,000	159	[4]
MDPBP	3	143	67	10,400	155	[2,3,5]
4Cl-α-PVP	1	70	8.0	1,070	134	[1]
MDPPP	3	1,240	423	42,000	99	[2,3,5]
4-Me-PPP	1	640	750	55,000	73	[2]
4C-α-PPP	1	764	569	10,000	17.6	[11]
Comparator compounds						
Cocaine	8	410	440	760	1.73	[12]
Methamphetamine	6	91	556	15,500	27.8	[12]
Mephedrone	8	470	2,350	3,690	1.57	[12]
Methylphenidate	5	99	85	169,000	1,988	[12]

Notes:

Values are means of cited studies.
IC_{50} is the concentration of compound needed to reduce transporter activity by 50%.
Lower numbers reflect greater potency
[1] Persson and others, 2024
[2] Kolaczynska and others, 2021
[3] Rickli and others, 2015
[4] Baumann and others, 2018
[5] Gannon and others, 2018
[6] Marusich and others, 2014
[7] Zwartsen and others, 2017
[8] Rickli and others, 2019
[9] Eshleman and others, 2013
[10] Meltzer and others, 2006
[11] Chojnacki and others, 2023
[12] Docherty & Alsufyani, 2021

13.5. Although α-PHP, MDPHP and α-PVP all have high DAT-to-SERT selectivity (that is, low SERT:DAT ratio), there is limited information on how addictive these substances might be (Zawilska and Wojcieszak, 2017). Behavioural studies with pyrrolidino-cathinones in rodents show they typically increase locomotor activity and are self-administered, which indicates abuse potential,

consistent with their actions as psychostimulants (Gatch and others, 2015; Javadi-Paydar and others, 2018; Marusich and others, 2021; Daziani and others, 2023; Jeon and others, 2024). Intravenous drug self-administration studies in rodents suggests that these compounds can be self-administered, evoke conditioned place preference (that is, drug-seeking behaviour), and can lower the threshold for intracranial self-stimulation (ICSS, suggesting a sensitised brain reward system). Of the synthetic cathinones tested, α-PHP appears to have the greatest addictive liability in these tests, but insufficient information is available on which to draw firm conclusions. MDPHP was unusual in not supporting drug self-administration in rats, though this was a single study (Pisanu and others, 2022).

13.6. MDPV and α-PVP were also tested against the established stimulants, cocaine and methamphetamine using an IV self-administration model in rhesus monkeys (Collins and others, 2019). Dose-response curves were constructed for each drug and the schedule of reinforcement was a progressive ratio, where the monkeys had to work harder and harder for each infusion. Progressive ratio schedules are considered the best test for reinforcing efficacy as a measure of abuse potential. It was found that both MDPV and α-PVP had greater 'breaking points' than cocaine and methamphetamine, thus the monkeys worked harder to obtain the 2 pyrrolidino-cathinones, and also took the drugs for longer. Concentration-response curves showed both MDPV and α-PVP to be effective reinforcers at lower doses. Taken together, these strongly indicate α-PVP and MDPV would each be at least as addictive as cocaine or methamphetamine in humans. The findings of this study are consistent with studies in rodents, which also examined the reinforcing strength of MDPV and α-PVP versus established stimulants (Watterson and others, 2014; Aarde and others, 2015; Gannon and others, 2017; Gannon and others, 2018).

13.7. Pyrrolidino-cathinones do not appear unusually cytotoxic, but few studies have looked in detail at this aspect (Lenzi and others, 2021; Sogos and others, 2021; Marusich and others, 2022).

Individual compounds

13.8. The available evidence of the unwanted health effects of individual synthetic cathinones of interest is reviewed below. Some reports suggest that adverse health effects may be more frequent or pronounced with some pyrrolidino-cathinones compared with other synthetic cathinones such as mephedrone. However, the overall numbers of reports of acute toxicity for each synthetic cathinone are small and there are no published cases for some examples. There is a particular a lack of research providing reliable information on comparative human health harms of different cathinones. The pattern of effects reported with pyrrolidino-cathinones appears to be similar to those seen with other cathinones and there is no conclusive evidence of increased toxicity associated with any specific example (Zaitsu and others, 2014; Zawilska and Wojcieszak, 2017; Kolesnikova and others, 2019).

MDPHP

13.9. This report considers MDPHP (3',4'-Methylenedioxy-α-pyrrolidinohexiophenone) in detail because of its common involvement in drug-related deaths and its detection in samples of ‘monkey dust’. Its detection was first reported in Europe in 2014.

13.10. In pharmacology studies, MDPHP potently inhibited DAT and NET with IC_{50} values of 50nM and 60nM respectively, with low-to-moderate inhibition of SERT (Table 5). MDPHP was unusual in not supporting drug self-administration in rats, though this was a single study (Pisanu and others, 2022). In a study using mice, MDPHP produced similar sensorimotor and behavioural responses to those of MDPV, with both compounds increasing locomotion and inducing aggressive behaviour. Increases in heart rate and blood pressure were observed with higher doses (Bassi and others, 2024).

13.11. The Swedish ‘STRIDA’ study involved the analysis of 2,545 biological samples taken from patients with acute drug intoxication between January 2011 and March 2016. Of these, 26 (1%) contained MDPHP, which was detected in the absence of co-used drugs in 4 cases. The clinical features in these included chest pain, breathing difficulties, tactile hypersensitivity, anxiety, dizziness, hypertension, aggression/psychosis and hallucinations (Beck and others, 2018).

13.12. MDPHP was detected in samples collected between February and June 2019 from 5 individuals presenting to an emergency department in Lower Saxony, Germany with acute drug toxicity; all had at least one other substance detected. Clinical features included drowsiness/coma, abnormal behaviour, aggression, confusion, psychosis and agitation (Grapp and others, 2020).

13.13. There is one case report of a 21-year-old female, 36 weeks pregnant, who collapsed and was agitated with mumbled speech, tachycardia and hypertension following lone MDPHP use (Adamowicz and others, 2019).

13.14. There were 17 presentations to a hospital in Florence, Italy between January 2022 and September 2023 where MDPHP was detected in blood and/or urine sent for routine toxicological screening because of suspected acute drug intoxication; the majority also had at least one other substance detected. Clinical features reported included restlessness/agitation, psychiatric symptoms, respiratory symptoms, neurological symptoms, tachycardia, elevated creatine kinase and hypertension (Arillotta and others, 2024).

13.15. In a further Italian case series, 56 cases of human intoxication were identified involving MDPV and/or MDPHP between 2010 and 2023. Of these, 45 involved MDPHP, with most identified between 2020 and 2023. Users were commonly men who have sex with men and were often polydrug users. The cathinones were usually smoked, snorted or ingested in the context of chemsex. Clinical features reported in MDPHP users included tachycardia (34.8%), rhabdomyolysis (23.9%), hypertension (13.0%), tremors or fasciculations (13.0%), respiratory disorders (13.0%), hyperthermia (8.7%), acidosis (10.9%), coma (10.8%), migraine (6.5%) and seizures (4.3%).

Psychiatric features were also common and included agitation (89.1%), paranoid behaviour (32.6%), auditory and visual hallucinatory experiences (28.3%), aggressive behaviour (21.7%), confusion (17.4%), delirium (10.9%) and anxiety (2.2%). Violent behaviour, sometimes requiring containment measures, was recorded in 8.7% of cases (Bassi and others, 2024).

13.16. There were 7 Euro-DEN Plus presentations between October 2013 and December 2022 after self-reported use of MDPHP, of a total of 71,463 presentations). These were in Belgium (3) and Finland (1), France (1), Poland (1) and the UK (1). Three reported lone MDPHP use, and the others also reported exposure to one or more other substances. Commonly reported features were neuropsychiatric (agitation, drowsiness, psychosis and hallucinations) and cardiovascular (tachycardia) (Wood and others, 2024a).

13.17. The Identification of Novel Psychoactive Substances (IONA) study detected MDPHP in samples from 3 of 1,815 UK ED patients studied between 2015 and 2023, 1 in 2017 and 2 in 2018. All were males attending the same ED in Blackpool. None reported the use of 'monkey dust' and all had other illicit substances detected in their samples. One man presented with tachycardia, extreme agitation and hallucinations after allegedly having his drink spiked. He recovered rapidly without specific treatment and was discharged after 8 hours. A second man presented with a reduced level of consciousness, seizures, tachycardia, pupillary dilatation and respiratory acidosis after reportedly smoking 'spice'. As well as MDPHP, 3 different SCRAs, 2 benzodiazepines and fentanyl were also detected in his biological samples. A third presented with a reduced level of consciousness, unresponsive to naloxone and severe respiratory acidosis after injecting a brown substance intramuscularly. As well as MDPHP, his blood and urine samples contained benzodiazepines and opioids, which were more likely to have caused his clinical features.

13.18. MDPHP was the only attributed substance detected in femoral blood in a 48-year-old Italian man who died suddenly after presenting to a hospital with mild tachycardia. MDPHP was also found amongst his possessions. (Di Candia and others, 2022).

α-PHP

13.19. Like other pyrrolidino-cathinones, α-PHP is reported to be a potent DAT and NET inhibitor (IC_{50} values of around 40 nM at each) with limited activity at SERT (Table 5).

13.20. α-PHP was first detected in Europe in 2014. There have been 2 reports of toxicological screening studies in South Bavaria and Lower Saxony, Germany between 2017 and 2021 reporting the detection of α-PHP in 53 police samples and 7 ED/psychiatry samples. In the majority of cases, other recreational drugs/NPS were also detected. The most commonly reported clinical features were being "slowed down", impaired balance/behaviour, aggression and agitation. Other clinical features included restlessness, drowsiness, confusion, disorientation, nausea, sweating, drowsiness and psychosis (Grapp and others, 2023; Brueckner and others, 2024).

13.21. Three further case reports describe α-PHP-related acute toxicity/harm. The first involved a 21-year-old female with paranoid psychosis and akathisia (feeling of inner restlessness associated with mental distress and the inability to sit still) after reported use of synthetic cathinones including α-PHP, α-PVP and α-PHiP; no toxicological screening was undertaken (Albert and others, 2022). The second was a 39-year-old male with hallucinations, agitation and delusions. In this case, toxicological screening only detected α-PHP (Fujita and others, 2018). The third case was a 38-year-old male with dilated pupils, tachycardia and dehydration, whose urine and gastric content samples contained α-PHP together with several other synthetic cathinones and synthetic cannabinoids (Klavž and others, 2016).

13.22. In the Swedish STRIDA project, there was a single detection of α-PHP between January 2011 and March 2016. This person experienced breathing difficulties, palpitations, jaw spasm, dilated pupils, hypertension and paraesthesia. Several other synthetic cathinones were also detected (Beck and others, 2018).

13.23. There were 8 Euro-DEN Plus presentations with self-reported α-PHP exposure between October 2013 and December 2022 , out of a total of 71,463 presentations. These were in France (4), the UK (2), Belgium (1) and The Netherlands (1) –All involved the use of one or more other recreational drug or NPS. Neuropsychiatric features seen included psychosis, hallucinations, aggression/agitation and seizures; cardiovascular features included palpitations, hypertension, tachycardia and chest pain (Wood and others, 2024b).

α-PVP

13.24. α-PVP was first detected in Europe in 2011. Like other pyrrolidino-cathinones, it has been shown to be a potent inhibitor of DAT and NET (IC_{50} values 30nM to 40nM) with little effect at SERT (Table 5). α-PVP has been found to increase inflammatory cytokines in the brain when administered to rats, though not to the same extent as mephedrone (Marusich and others, 2022). This suggests that this compound might be neurotoxic, although less so than mephedrone.

13.25. There is animal evidence suggesting abuse potential for α-PVP. In rodents, acute administration evoked dose-dependent hyperlocomotion, while those trained in the intravenous α-PVP self-administration model show constant drug intake. The drug also produces dose-dependent conditioned place preference (Kolesnikova and others, 2019), which is a behavioural model that measures reward by assessing an animal's preference for a location where a rewarding event (such as a drug) is present. In rhesus monkeys, α-PVP supported self-administration more effectively than cocaine or methamphetamine, with a high level of response for an extended time (Collins and others, 2019).

13.26. Human use of α-PVP became common in North America in the later 2010s, where the drug was often referred to as 'flakka'. Preparations included crystals, tablets, capsules, powders, liquids, blotters, and 'gummies', with

routes of administration described including ingestion, nasal insufflation, injection, sublingual, and rectal. It is described as having rapid absorption with effects in humans occurring within 10 minutes, peaking after 10 to 40 minutes and lasting 2 to 3 hours (Kolesnikova and others, 2019).

13.27. Effects of α-PVP use include euphoria, elevated mood, alertness, pleasurable rush and sexual stimulation; but paranoia, hallucinations, psychosis-like states, bizarre behaviour, agitation, increased aggression/violence, myoclonus and seizures may occur. Tachycardia, hypertension, chest pain, cardiac arrest and dysrhythmias are also described. Thermoregulatory deficits also commonly occur after α-PVP intake, as evidenced by records from surveillance cameras showing α-PVP users removing clothes to cool themselves down (Kolesnikova and others, 2019; Patocka and others, 2020).

13.28. In the Swedish STRIDA project, α-PVP was the only stimulant detected in 42 cases screened between 2012 and 2015. Of these, 13 were lone α-PVP exposures and the remainder had one or more non-stimulant substances detected. Clinical features reported included tachycardia, hypertension, hallucinations, delirium and drowsiness (Beck and others, 2018).

13.29. A 19-year-old male was brought to the ED in Spain with tachycardia, agitation, bruxism, delusions and paranoia following the lone use of α-PVP (Quesada and others, 2016).

13.30. α-PVP has been detected in samples taken in suspected drug-related death cases, with 115 deaths involving α-PVP recorded between 2012 and 2015 across 8 European Union member states (Karila and others, 2018). In most cases, other substances were also identified, but there were 5 cases where α-PVP was the only substance identified.

Other cathinones

Dibutylone

13.31. Dibutylone is not a pyrrolidino-cathinone but is considered in this report because of its involvement in several recent suspected drug-related deaths in the UK. It was first reported in Europe in 2010 after detection in Finland, and subsequently became the most common phenethylamine compound detected in Sweden. In 2018, it was the third most common cathinone detected by the US Drug Enforcement Administration’s laboratory system (DEA, 2018).

13.32. The potency of dibutylone for inhibition of neurotransmitter uptake, studied in human embryonic kidney cells, was intermediate between mexedrone and several pyrrolidino-cathinones, with IC_{50} values of 0.3μM, 0.9μM and more than 9.7μM at DAT, NET and SERT, respectively. It did not show activity as a 5-HT releaser (Eshleman and others, 2019). It is a weak motor stimulant compared to cocaine, methamphetamine and MDMA (Gatch and others, 2019) but can maintain drug self-administration, albeit with less efficacy than methamphetamine (Lai and others, 2022).

13.33. There is limited evidence available about the effects of dibutylone in humans. There are no published cases of human toxicity, but dibutylone was detected in samples from 14 individuals (10 male) that were analysed in the US in 2018. In fatal cases, dibutylone concentrations ranged from 10ng/ml to 1,400ng/ml (median 27). While other substances were also commonly identified, there were at least 2 fatal cases where no other substances were identified (Krotulski and others, 2018). In 2023, dibutylone was detected alongside other synthetic cathinones in blood samples taken from people in Victoria, Australia, who had reported the intended use of MDMA (Victoria Department of Health, 2023).

Uncontrolled synthetic cathinones

13.34. Synthetic cathinones detected in Europe but not captured by the current UK generic text are listed in Table 6. Seven of these compounds have also been detected in the UK. There is little published information on their pharmacology or the human health harms associated with their use, but the limited detail that is available is summarised in Table 6.

13.35. The lack of published case reports or case series does not mean that these substances are not associated with acute toxicity or other harms; other factors such as publication bias and/or confounding from other co-used substances may have prevented the publication of any cases of acute toxicity or other harms related to these substances.

13.36. There are also several ‘iso-cathinone’ compounds, with reversed amino and keto components, reported in Europe but not listed in the table or dealt with further in this report because they are likely to be unintended synthetic by-products and are all probably of low activity. These are iso-ethcathinone, iso-pentedrone, 3F-iso-methcathinone, iso-3-CMC, iso-(meta-methyl-propcathinone) and iso-3-MMC.

13.37. Two related compounds have also been reported in Europe, βk-2C-B and BOH-PHP. Although structurally similar, these are not cathinones and are therefore outside the scope of this report. βk-2C-B has some activity at the 5-HT_{2A} receptor (Åstrand and others, 2020) and is a weak MAO-B inhibitor with an IC_{50} of 14μM (Wagmann and others, 2019). BOH-PHP is a known metabolite of α-PVP but has also been detected in a powder sample. No further action is required currently beyond routine monitoring for their appearance in UK drug markets.

Table 6. Synthetic cathinones detected in Europe that are not captured by the current UK generic text

Name	IUPAC name	UK detections?	Pharmacology	Harms
(a) Benzyl group attached to amine nitrogen				
Benzedrone	1-(4-methylphenyl)-2-benzylamino-propan1-one	Yes	Weakly active at DAT, NET and SERT (Iversen and others, 2013)	No published human information
N-methyl benzedrone	1-(4-methylphenyl)-2-(benzyl(methyl)amino)-propan-1-one	Yes	No information available	No published human information
BMDP	1-(3,4-methylenedioxyphenyl)-2-benzylamino-propan-1-one	Yes	Weakly active at DAT, NET and SERT (Iversen and others, 2013)	No published human information
BMDB	1-(3,4-methylenedioxyphenyl)-2-benzylamino-butan-1-one	No	No information available	No published human information
4'-methyl buphedrone, *N*-benzyl derivative'	1-(4-methylphenyl)-2-benzylamino-butan-1-one	No	No information available	No published human information
(b) Cycloalkyl group attached to the amine nitrogen, rather than an alkyl group (IUPAC definition of 'alkyl' excludes cycloalkyl)				
3,4-dichloro-*N*-methyl-*N*-cyclohexylcathinone	1-(3,4-dichlorophenyl)-2-cyclohexyl(methyl)amino-propan-1-one	No	No information available	No published human information
N-Cyclohexylmethylone	1-(3,4-MDO-phenyl)-2(cyclohexyl(methyl)amino)-propan-1-one	Yes	No information available	No published human information
N-cyclohexylnor methylone	1-(3,4-MDO-phenyl)-2-cyclohexylamino-propan-1-one	Yes	No information available	No published human information

Name	IUPAC name	UK detections?	Pharmacology	Harms
N-cyclohexylnor butylone	1-(3,4-MDO-phenyl)-2-(cyclohexylamino)-butan-1-one	Yes	No information available	No published human information
(c) Methoxy extension to the alkyl sidechain, which is not covered by the generics				
Mexedrone	1-(4-methylphenyl)-2-methylamino-3-methoxypropan-1-one	Yes	Very modest activity at DAT (6.8μM), NET (8.8μM) and SERT (5.2μM) in rat synaptosomal preparations (McLaughlan and others, 2017). Evokes 5-HT efflux with an EC_{50} of 2.5μM (much less potent than mephedrone, which has IC_{50} values of 0.23, 0.05 and 29.4μM at DAT, NET and SERT respectively (Eshleman and others, 2019).	Detected in 11 out of 305 (3.6%) patients who presented to a hospital in Birmingham, UK, between December 2015 and July 2016 with suspected drug use. Besides mexedrone, all had at least one other drug or NPS detected on urine toxicological screening. Clinically significant features reported included agitation, confusion, tachycardia and palpitations, coma, paranoia, dizziness, delusions, pyrexia, bradycardia and hypertension. Urine mexedrone concentrations ranged from less than 10ng/mL to 3,538ng/mL (Roberts and others, 2017).
3-Methoxy-α-PPP	(1-phenyl-2-pyrrolidin-1-yl)-3-methoxypropan-1-one)	No	No information available	No published human information
(d) Third carbon atom of the sidechain incorporated into a cyclic structure, which is outside the scope of the generics				
Indapyrophenidone	1-(2,3-dihydro-1-H-inden-5-yl)-2-(pyrrolidin-1-yl)-2-phenyl ethan-1-one	No	No information available	No published human information

Name	IUPAC name	UK detections?	Pharmacology	Harms
α-PCyP	2-cyclohexyl-1-phenyl-2-(pyrrolidine-1-yl)-ethan-1-one	No	Limited data available suggests that α-PCYP is around twice as potent as α-PVP at DAT and had little-to-no activity at SERT (Kolanos and others, 2015)	No published human information
α-D2PV	1,2-diphenyl-2-(1-pyrrolidinyl)-ethan-1-one	Yes	Structurally related to diphenidine	Euphoria, stimulation, increased libido, vasoconstriction, anxiety, and the inability to focus reported in the user (Kuropka and others, 2023a)

14 Conclusions

14.1. Use of synthetic cathinones has been declining in the UK in recent years, mainly driven by a reduction in prevalence of mephedrone use since 2010. The number of deaths involving mephedrone has been falling since 2015. Since then, there has been an increase in the proportion of deaths involving other cathinones, but absolute numbers of deaths remain low compared to those involving other substances of misuse such as heroin or cocaine and have not increased recently.

14.2. Other than mephedrone, the synthetic cathinones most commonly involved in drug-related deaths in the UK over the last 5 years have been MDPHP, α-PHP and α-PVP, all pyrrolidino-cathinones, as well as dibutylone. Involvement of these compounds in drug-related deaths could reflect their toxicity or their frequency of use, however, their detection in cases of drug-related death does not mean that they are the cause of death, as other compounds are almost always identified alongside them.

14.3. There are pharmacological reasons to suggest that pyrrolidino-cathinones may have more marked psychostimulant effects and abuse liability compared to other cathinones such as mephedrone. These include the potency of their actions as DAT and NET inhibitors with their associated low SERT:DAT ratios and their increased lipid solubility, which may increase penetration into the brain. While a low SERT:DAT ratio may not be a consistently reliable indicator of high abuse liability, there is also accumulating evidence that some pyrrolidino-cathinones display increased re-enforcing effects in primates, which is consistent with more severe dependence liability. The animal research studying cathinone toxicology, however, is incomplete.

14.4. Very limited human data exists from which to draw reliable conclusions about the relative toxicity of pyrrolidino-cathinones compared to other cathinones. Comparisons in humans are problematic because observed toxicity may be influenced by other factors besides the specific cathinone involved, such as the dose of the product used, the purity of the preparation, the route of administration and the effects of other substances as multiple exposures are common. In relation to dose, it is not possible to know if producers are diluting appropriately these more potent drugs with excipients to ensure that dosing delivers appropriate amounts of the cathinone needed to obtain the desired effects without causing toxicity. There are reports of pyrrolidino-cathinones producing marked psychostimulant effects, but these are also described with other cathinones, and it is not possible to demonstrate with certainty that the risk of adverse outcomes from human use is higher with pyrrolidino-cathinones. Data provided for this report by UK stakeholders suggests a disproportionately high representation of pyrrolidino-cathinones in PM toxicology cases compared with drug seizure or submitted sample analysis. Interpretation is difficult, however, because the numbers involved are relatively small, seizure or submitted samples counts do not necessarily reflect prevalence of population use, and deaths where compounds are detected at PM may be caused by co-used drugs.

14.5. There are particular concerns about synthetic cathinone use in North Staffordshire and the surrounding areas, where the use of ‘monkey dust’ is commonly reported and associated with antisocial behaviour, with substantial effects on local communities. From the limited testing performed, ‘monkey dust’ has been found to contain various pyrrolidino-cathinones, specifically MDPHP, α-PiHP or α-PHP, sometimes with other substances of misuse.

14.6. Drug-related deaths involving pyrrolidino-cathinones are much more common in North Staffordshire and surrounding areas than elsewhere in the UK and deaths in that geographic area account for most drug-related deaths in the UK involving a pyrrolidino-cathinone, with the compounds most commonly involved being MDPHP, α-PHP and α-PVP. The reason for this high local concentration of use and harms in relation to these compounds remains unclear.

15 Legislative options

15.1. Synthetic cathinones appearing in illicit drug markets, including the pyrrolidino-cathinones found in ‘monkey dust’, are almost all currently classified under the MDA as Class B. In view of their involvement in ‘monkey dust’ preparations and the effects of these substances on local communities, as well as their association with suspected drug-related deaths in the UK, it is appropriate to consider the arguments in favour of for and against changing classification to Class A for selected examples.

15.2. The lower sentencing for possession and supply offences (Table 7) for Class B compared with Class A drugs means that criminal enterprise involving the former is effectively lower risk and high yield and there may be insufficient deterrent. Courts use Criminal Sentencing Guidelines, which specify the factors they should use in considering appropriate sentences. These are often less severe than the maximum penalties shown in Table 7. Reclassification of some or all synthetic cathinones to Class A would ensure greater sentencing powers for the court, potentially providing an increased deterrent for would-be offenders, focusing particularly on those within supply chains. It is not clear, however, how great the deterrent would be, especially for those importing or supplying synthetic cathinones alongside Class A drugs such as heroin or cocaine.

Table 7. Maximum penalties for drug possession, supply (selling, dealing or sharing) and production according to MDA drug class

	Maximum penalties	
MDA class	**Possession**	**Supply and production**
Class A	Up to 7 years in prison, an unlimited fine or both	Up to life in prison, an unlimited fine or both
Class B	Up to 5 years in prison, an unlimited fine or both	Up to 14 years in prison, an unlimited fine or both
Class C	Up to 2 years in prison, an unlimited fine or both*	Up to 14 years in prison, an unlimited fine or both

* Except anabolic steroids – it is not an offence to possess them for personal use.

15.3. It has been suggested that a higher classification under the MDA might also increase the priority for action by police and Border Force, not just in areas where synthetic cathinone use is prevalent, and this may help disrupt supply chains. Law enforcement tasking processes, from local to regional, are driven by a monthly Tasking and Coordination Group with threats evaluated using the Management of Risk in Law Enforcement (MoRILE) tool. This is a purist and evidential approach to prioritisation, supporting location of a priority grading and tasking a response to an appropriate owner, such as a local police force, Regional Organised Crime Units or the National Crime Agency. A MoRILE score is an ongoing cyclical review process which involves scores determined by a range of factors including impact and harm (to victim, community or environment), threat (intent, capability, geographic, frequency and volume), confidence and organisational position (priority, reputation, resourcing). Reclassification of a drug from Class B to Class A would not specifically influence MoRILE scoring. Classification of a drug may be a factor in determining operational priority, but other key factors determining the impact of the threat on the region (such as harm and scale) are also considered.

15.4. One aspect factored in by MoRILE scoring is the geographic impact of a threat. Work has been conducted in Stoke to assess MoRILE scoring, comparing operations involving ‘monkey dust’ with those involving Class A drugs to identify how scores are impacted by current classification. This demonstrates that in Staffordshire, ‘monkey dust’ features highly in drug assessments and above most Class A drugs because of the vulnerability of people using it and the harms it produces for individuals and the community. These include behavioural effects in people using ‘monkey dust’, the more regular supply/demand requirements associated with its short duration of action, and intermittent incidents of higher physical harm, violence, sexual assaults and/or exploitation.

15.5. A drug impacting a single force area or contained geographic area, however, is less likely to be adopted at a regional or national level and would likely be owned locally. This is an important consideration because of the localised nature of ‘monkey dust’ use. Police and partners recognise MDA Class A drugs as a greater overall threat and risk than those in Class B, and there is a public expectation that police focus on the greater risk to communities.

15.6. Arguments against reclassification of some or all synthetic cathinones to Class A also include:

a) The risk they pose to public health is limited and has been declining overall. Use and harms associated with synthetic cathinones has become less common across the UK in recent years. Although pyrrolidino-cathinones have caused significant problems in and around North Staffordshire, their use appears uncommon elsewhere, especially when compared with other substances.

b) Unlike many Class A drugs, synthetic cathinones are not associated with high rates of acquisitive crime, with the main societal impact restricted to antisocial behaviour and the use of policing and healthcare resources to deal with this. If reclassification resulted in increased supply costs, the

risk of acquisitive crime to fund drug purchases could increase. The removal of legal and cost differentials could encourage some synthetic cathinone users and their suppliers to switch to potentially more hazardous Class A compounds, such as cocaine.

c) Reclassification may increase stigma for people using these drugs, discouraging them from seeking social or medical support. Their further criminalisation may present additional barriers to accessing services such as housing.

d) Reclassification of some (but not all) synthetic cathinones to Class A would require changes to the generic text so that the descriptions of chemical structures and modifications are specific to each class. While this may be possible, it makes the legislation increasingly complex, and this may be confusing for people who use drugs, enforcement agencies, the public and other stakeholders.

e) Reclassification would not affect MoRILE scoring and as such would not necessarily increase the priority for action by police forces, especially in places where use of reclassified compounds was not common.

f) There is a risk that reclassification of some compounds would impact on their possible future use in research, including in the development of new medicines.

15.7. There are a few synthetic cathinones detected in the UK or Europe that are not captured by the current generic text and are therefore not controlled via the MDA. Very limited information is available on the pharmacology or health harms associated with these compounds and currently their prevalence in the UK is low. Two have been recorded in drug-related deaths, although it should be noted that this does not necessarily mean that they caused or contributed to the death. One compound, α-D2PV, has pharmacological similarities to diphenidine and has caused clinical toxicity. This compound should, therefore, be considered for classification via the MDA.

16 Other options

16.1. More widely, a public health approach, in line with the National Drug Strategy and the recommendations of the Home Affairs Select Committee (2023), is more likely than changes to legislation to impact synthetic cathinone use. This should include early identification of vulnerability, assisting people out of poverty and a joined-up rehabilitation landscape, including referrals into effective treatment across a broad range of public agencies, not just law enforcement. This would also help to reduce the repeat offending cycle within which many individuals find themselves. Structural factors, and inequalities, and their links to substance abuse (Addison, 2023) should not be overlooked. The available research (McCormack and others, 2023a) and the responses from stakeholders to our Call for Evidence suggest that services, including access to accommodation, mental health support and ambulance response services are compromised by stigma and organisational resource challenges.

16.2. With the links between homeless populations and the use of ‘monkey dust’, the Housing First model may offer a way forward to address synthetic

cathinone-related harms. Housing First places people experiencing long-term homelessness in accommodation, rather than offering housing as a reward for adhering to treatment and support plans (Tsemberis and others, 2004). It acknowledges that people have the right to a home, and that recovery is not linear, making compassionate allowances for when someone regresses on their recovery journey. The Housing First model can be framed as a health intervention by preventing further deterioration (Wood and others, 2019) and providing the conditions needed to begin recovery from long-term homelessness. The model is typified by smaller caseloads for support staff and holistic intervention. Evaluations of Housing First in England have reported promising results in terms of tenancy sustainment (Homeless Link, 2015), outcomes relating to mental and physical health, alcohol and substance misuse (Bretherton and Pleace, 2015), and cost effectiveness (Pleace and Bretherton, 2019). A meta-analysis identified studies that evidenced decreases in drug use for Housing First customers and strong evidence supporting significant improvement of their mental health (Spyropoulos and others, 2022). The ACMD has previously reported on the effectiveness of this model and recommended that strategies and plans across the UK should specifically address the needs of people who use drugs and are experiencing homelessness by recommending evidence-based housing provisions, such as Housing First. This will enable collaboration across departments and agencies to ensure these interventions have a chance to succeed (ACMD, 2019).

16.3. Improved access to mental health and drug treatment services are needed, with availability of appropriate routes of referral to each, both in the community and in (or leaving) prisons, and these should include services suitable for young people. While there are no substitute licensed medicinal drugs effective for treating people who use synthetic cathinones, talking therapies (for example, interventions deriving from the cognitive behavioural approach) may be effective and further evaluation of this approach for synthetic cathinone users is needed to gain a more nuanced understanding of their effectiveness. Evidence submitted to this review suggests that having a dedicated worker providing talking therapies may be effective in addressing issues, but more research is needed to produce a robust evidence base on which to plan effective interventions. Supporting local authorities to better resource the services they commission for co-occurring mental health and drug and/or alcohol use could help to address the challenges the police are facing when working with synthetic cathinone users.

16.4. The DIVERT early intervention programme is an interesting approach that could be used for young people arrested in connection with the use of synthetic cathinones and other substances. DIVERT aims to educate and inform them to make informed choices about their drug use. Young people can engage with the programme by asking to see a locally based DIVERT specialist Custody Intervention Coach while in the custody suite. The coaches focus on long-term personal plans, which can include training, education and employment, and access to other services and a supportive environment community through sport, music and more (Bounce Back, 2024). Evaluations of DIVERT programmes have, however, produced mixed results, without consistent reductions in rates of re-arrest (College of Policing, 2021). There

are, however, methodological challenges to evaluations and ongoing refinement, and further evaluation of DIVERT interventions appears necessary.

16.5. The ‘Safer Streets’ initiative is a programme that aims to reduce serious harm and increase public confidence in policing and in the criminal justice system, with priorities including combatting knife crime and violence against women and girls. It involves putting increasing numbers of police officers, PCSOs and special constables into neighbourhood policing roles. One important aim of the initiative is to tackle anti-social behaviour with an improved neighbourhood policing response. There are advantages to the provision of resources from this initiative towards areas where drug use and associated antisocial behaviour and other criminality is prevalent.

16.6. Guidance regarding Drug Treatment Orders by the Court at the point of sentencing to mandate people who use synthetic cathinones to engage with rehabilitation programmes may be useful and should be explored further.

16.7. Parents have reported that having public health messaging around ‘monkey dust’ would be helpful for safeguarding conversations with their children (McCormack and others, 2023a).

16.8. Creating safe spaces for people to go to when in drug and mental health crisis may also help to reduce harms, especially if there is improved access for mental health support (McCormack and others, 2023b). Such actions would be costly and would require additional government funding.

16.9. There is a need for appropriate services in affected communities for those affected by sexual violence besides the national online or telephone support services such as Victim Support, Rape Crisis helpline, Survivors Trust and National Male Survivor helpline and online service. These should include adequate resources and trained sexual assault referral centres.

16.10. Greater levels of surveillance in neighbourhoods more affected by ‘monkey dust’, including the increased use of CCTV and foot patrolling, may help residents to feel safer and could assist with obtaining greater numbers of immediate prosecutions as a measure to safeguard a community; however, displacement of drug dealing may well occur (McCormack and others, 2023a; Page and Griffin, 2023).

16.11. Increasing policing at community level would seemingly benefit the flow of intelligence gathering and likelihood of prosecutions to better safeguard the local community (McCormack and others, 2023a; Page and Griffin, 2023). However, greater surveillance requires appropriate resourcing; police are already finding policing synthetic cathinone-related issues to be time consuming and resource intensive.

16.12. Research is needed to develop better field testing so that police forces and other services can more easily identify synthetic cathinones. The current limited understanding of the compounds involved in illicit drug preparations, such as ‘monkey dust’, limits the ability to identify patterns that might be present, which could be useful to those working with people using the drugs, to law enforcement and to healthcare providers. Eurofins Forensic Services screen most of their samples using simple colour tests such as the Marquis Reagent, which is currently approved for use by the Evidential Drug

Identification Testing (EDIT) process used by police. Methylenedioxy-cathinone derivatives, such as MDPHP, give a bright yellow colour change with this test. This, however, is not specific and several methylenedioxy-cathinones give the same yellow colour change, while this is not observed for other cathinones, such as α-PVP. Testing confirms that it is the methylenedioxycathinones that react and not an associated cutting agent, such as caffeine. Suitable verification testing will be required by the Home Office or Defence Science and Technology Laboratory (DSTL) prior to this colour change being allowed to indicate a methylenedioxy-cathinone for use by the police. Its introduction to the EDIT process or similar testing could be used under appropriate testing conditions. This is being considered by the Forensic Science Regulator's Drug Test Kit working group.

16.13. It remains essential that there is close monitoring of the use of NPSs in the UK and their adverse health effects. The involvement of NPSs in drug-related deaths is a particularly important measure reflecting serious health harms. Because of this, ACMD has made recommendations in several previous reports aimed at strengthening the quality and consistency of PM forensic analysis, as it is essential that analysis can detect recently encountered NPS if their impact is to be tracked. ACMD is aware of and supports the current work of the Office for Health Improvement and Disparities (OHID) and Public Health Scotland in developing relevant data sets, including drug seizure data, submitted sample analysis, ED presentations and PM toxicology, as well as their ongoing work with coroners and forensic toxicologists to enhance the standards of PM toxicology testing.

16.14. It is also important that the UK can monitor the emergence of NPSs in Europe, as there is a high risk that compounds appearing in neighbouring countries will also appear in the UK. There are also advantages to joint working with neighbouring countries to avoid duplication of effort in assessing risks associated with these compounds. The current lack of joint working with EUDA and of access to their European New Drugs Database (ENDD) disadvantages UK stakeholders involved with tracking NPSs and responding to their associated public health challenges, restricting information on use in Europe and requiring duplication of work on chemistry, pharmacology, toxicology, and health and social harms.

17 Recommendations

No recommendation on its own, including changing classification under the Misuse of Drugs Act 1971, is likely to be sufficient to substantially reduce the harms associated with use of synthetic cathinones, particularly where use and harms are localised to specific regions.

ACMD has the following recommendations, which the government should consider as a package of interventions. These include:

a) Changes to the Act by revision of the generic text for cathinones.
b) Improved health and social care for those with drug use disorders involving synthetic cathinones and other substances.

c) More effective use of law enforcement and the criminal justice system to direct drug users to health and social care services, with expansion of policy initiatives, such as Safer Streets.
d) Improved education and training for users, the public and healthcare professionals.
e) Increased monitoring, surveillance and research funding in relation to synthetic cathinones and other novel psychoactive substances.

These recommendations build on advice provided by ACMD in previous reports across several of these topics, including 'Commissioning impact on drug treatment' (ACMD 2017), 'Drug-related harms in homeless populations and how they can be reduced' (ACMD 2019a), 'Ageing cohort of drug users' (ACMD 2019b) and 'Custody-community transitions' (ACMD 2019c).'

Changes to the Misuse of Drugs Act 1971

(A) Synthetic cathinones currently captured by the UK generic text:

The ACMD acknowledges the evidence that some synthetic cathinones are of particular concern because they are (a) highly potent as DAT and NET inhibitors, (b) may have greater reinforcing properties compared to cocaine and methamphetamine, and (c) can be associated with more severe health harms than others, including increased risks, clinical reports of severe or prolonged behavioural disturbances and of dependency. These adverse effects in users are disproportionately highly represented in post-mortem (PM) toxicology cases compared with drug seizure or submitted sample analysis. Adverse effects associated with their use may also cause significant harms to local communities. The specific pyrrolidino-cathinones involved, such as MDPHP, MDPHP, α-PHP, α-PVP and α-PiHP, have been most frequently encountered in North Staffordshire and its environs as components of 'monkey dust' preparations. These compounds are also detected more commonly there in drug-related deaths. The ACMD has therefore considered carefully whether these compounds require a higher classification within the MDA.

RECOMMENDATION 1: All synthetic cathinones captured by the UK generic text remain Class B (MDA) and Schedule 1 (MDR) materials.

While there is some evidence of increased health harms with some specific synthetic cathinones, this evidence is incomplete and there is a particular paucity of evidence of increased harms in humans compared with other compounds in Class B including amphetamines and desoxypipradrol.

The ACMD is particularly concerned about the health and social harms associated with pyrrolidino-cathinones in North Staffordshire and its environs; however, the evidence indicates that this is a localised problem. The overall public health impact of synthetic cathinone misuse across the UK has been declining, and the numbers of drug-related deaths associated with pyrrolidino-cathinones remains low and is not increasing.

Classification of implicated cathinones as Class A would increase sentencing powers for courts and may increase the priority for action by police forces nationally and by Border Force. The impact of this in deterring import, supply or use of these compounds in North Staffordshire and elsewhere is uncertain, however, especially as many suppliers and users are already involved with other Class A substances.

There are potential disadvantages of making specific compounds Class A, including further increasing stigma for users and potentially restricting their access to health and social care support, including housing.

It is also important to avoid the unintended reclassification of compounds with potential legitimate use, including medicines in development, as Class A compounds, because of the potential adverse impacts this may have.

The ACMD is unanimous in considering that the disadvantages of reclassification outweighed any possible advantages and believes that the ongoing problems with synthetic cathinones reported from North Staffordshire would be more effectively addressed by a public health, rather than a criminal justice approach, as detailed in the further recommendations below.

The available information on the pharmacology and health harms of dibutylone was also studied carefully. This compound was not considered to be sufficiently pharmacologically distinct or associated with increased health harms compared to other non-pyrrolidinocathinones to merit changing its current classification under the MDA.

(B) Synthetic cathinones not currently captured by the UK generic text:

RECOMMENDATION 2: Following appropriate consultation, the UK generic text for cathinones in the MDA should be updated, so that selected psychoactive cathinones that are not currently captured by the current text are included as Class B, Schedule 1 compounds.

The generic text for synthetic cathinones has been successful in capturing the great majority of synthetic cathinones encountered over the last 14 years. There are, however, some synthetic cathinones outside the scope of the generic text for which there is some evidence of psychoactivity and that have been encountered in the UK and/or Europe. The prevalence of use of these compounds in the UK is currently low and the evidence of harms associated with them is currently weak. Nevertheless, the advice is that there is sufficient evidence that one of these, α-D2PV, has the potential to cause health or social harms commensurate with classification in Class B because of its pharmacological similarity to diphenidine. There is also a potential future risk from compounds structurally related to α-D2PV, which is where the third carbon atom of the sidechain is incorporated into a cyclic structure. For this reason, adjustment of the current generic text to include such compounds in Class B is considered the most appropriate approach.

There are other synthetic cathinones detected in the UK or in Europe that are not captured by the current generic text, but the ACMD's advice is that there is currently inadequate evidence of prevalence in the UK, psychoactivity or risk of health or

social harms for control under the MDA to be justified at present. Psychoactive examples are currently subject to the provisions of the PSA (2016).

Proposed updated text, with an explanation, for the generic control of synthetic cathinones is provided in Annex D.

It is essential to avoid the unintended classification of compounds with potential legitimate use, including medicines in development, as Class B compounds. A consultation with appropriate stakeholders is therefore necessary before changes to legislation are made. These should include academia and the chemical and pharmaceutical industries.

Should it not be possible to draft generic text without risking capture of compounds for which there may be a potential legitimate use, the specific cathinone of current concern could be controlled as Class B by name. This compound is α-D2PV (see Table 6 or Annex A for its IUPAC name).

Lead: Home Office

Measure of outcome: The inclusion of the described compounds in Class B of the Misuse of Drugs Act 1971 and Schedule 1 of the Misuse of Drugs Regulations 2001, following appropriate consultation.

Improved health and social care for those with drug use disorders involving synthetic cathinones and other substances

Poverty and social deprivation are major factors underlying drug use, including use of synthetic cathinones, and this also applies to affected communities in North Staffordshire and its environs. Measures to address social deprivation more generally are likely to result in reduced drug use and less antisocial behaviour, but detailed recommendations are beyond the scope of this specific review.

A joined-up public health approach is needed to address the complex needs of people with drug use disorders involving synthetic cathinones, as well as other substances.

These compounds are often used with other illicit substances, including strong opioids or crack cocaine. Affected people also commonly have underlying mental health conditions, sometimes arising from previous trauma. They need timely and barrier-free access to effective drug treatment and mental health provision, involving clear referral pathways that avoid the risk of clients falling between different services.

In view of the association between homelessness and the use of synthetic cathinones, provision of appropriate housing should be considered a priority.

RECOMMENDATION 3: Healthcare commissioners, local authorities and other social care partners, NHS Mental Health Trusts, and other providers of mental health and/or drug treatment services should review local services and their referral pathways to ensure that they adequately encompass those consuming synthetic cathinones. Specifically, these services and their staff should be aware of the latest evidence on harms, as contained in this report, and their

care pathways must be accessible and able to provide high-quality care for those living with relevant mental health and drug use disorders.

In line with the National Drugs Strategy, adequate and appropriate drug treatment and mental health referral pathways are required to provide necessary care, including with resourcing, to meet locally relevant demand. These services need to be responsive to clients with complex needs, including those with drug use in the context of complex mental health issues. Services should be able to provide evidence-based and holistic care, including to those with multiple needs, and there should be clear referral pathways according to that need. High-quality collaboration, appropriate information sharing, and liaison between different services is essential. These referral pathways should be available without unnecessary barriers to those working in primary care, secondary care (including emergency departments), social services, the police, and the courts, and should adopt a facilitatory, patient-first approach, centred on the needs of the individual requiring care.

Service providers should consider the appointment of dedicated healthcare workers who can provide appropriate therapies to those with drug use disorders, including those affected by synthetic cathinone use. These should be informed by the latest evidence on harms and treatments, such as that contained in this report. They should also consider the establishment of safe spaces for those in crisis, with access to relevant mental health support.

Appropriate services encompassing physical and mental health needs should be available for those affected by, or vulnerable to, sexual and other forms of direct and indirect violence, harm, and exploitation.

This builds on recommendation 3 of the previous ACMD report ‘Drug-related harms in homeless populations and how they can be reduced’ (ACMD 2019a), which encourages evidence-based approaches to engage and retain homeless people in proven treatments. It is also consistent with recommendations provided in the ACMD report ‘Commissioning impact on drug treatment’ (ACMD, 2017), that it remains essential to maintain and protect budgets for drug and alcohol misuse services and to strengthen links between local health and social care systems and drug misuse treatment.

Leads: Department of Health and Social Care, working with NHS England and the Association of Directors of Public Health, Office for Health Improvements and Disparities, Joint Combatting Drugs Unit, local authorities and Integrated Care Board (ICB); Integrated Joint Boards; Regional Partnership Boards; or Health and Social Care Trusts that variously commission mental health and drug treatment services across the devolved nations.

Measure of outcome: Demonstration of clearly defined services supported by dissemination of relevant information, such as that provided in this report, and published referral criteria and pathways that establish working relationships which genuinely put individuals at the centre of their care. ICBs, or their equivalents noted above, would seem appropriate owners of this role, though they might wish to delegate them in certain circumstances to provider organisations.

RECOMMENDATION 4: The 'Housing First' model should be used to tackle homelessness in deprived communities, including amongst those with drug use disorders such as synthetic cathinone use. Adequate resource should be made available to allow this to happen.

Tackling drug use by homeless people is unlikely to be successful while they remain without appropriate accommodation. Dealing with their homelessness should be considered a priority.

The Housing First model provides permanent housing associated with open-ended support, allowing other issues, including drug use, to be addressed from a stable home platform. The ACMD has previously reported on the effectiveness of this model and recommended that strategies and plans across the UK should specifically address the needs of people who use drugs and are experiencing homelessness by: recommending evidence-based housing provisions, such as Housing First; enabling collaboration across departments and agencies to ensure these interventions have a chance to succeed (ACMD, 2019).

There continues to be a need for the Housing First model to be widely available, but especially in areas where homelessness associated with drug use is prevalent. This requires adequate resource, which usually comes from local authority commissioning, public health and adult social care or charitable sources. Government should consider the current resource available for Housing First programmes and ensure that this is sufficient for these programmes to be effective in these areas.

Continuation or extension of the Rough Sleeping Drug and Alcohol Treatment Grants should be considered to support homeless drug users by provision of accommodation together with drug and alcohol treatment and other support, such as access to mental health and substance dependence workers and peer mentors.

Leads: Ministry of Housing, Communities and Local Government; local authorities; housing associations; Department of Health and Social Care; OHID; equivalents in devolved administrations.

Measure of outcome: Establishment or enhancement of Housing First programmes in areas affected by synthetic cathinone use.

Law enforcement and the criminal justice system

RECOMMENDATION 5: Drug users in contact with the criminal justice system should be directed towards appropriate health and social services using established referral pathways, when this is appropriate.

Contact with the criminal justice system offers an opportunity to direct drug users towards appropriate services, with the aim of dealing with potentially reversible factors underlying their drug use and criminal or antisocial behaviour. This may result in contact with drug treatment services or actions to address social issues.

Support programmes for young people under arrest, such as the DIVERT programme, should be available. Their impact on subsequent criminal behaviour should be monitored.

For drug users involved with minor crimes who are encountering the police, and whose pattern of drug use or degree of dependency is sufficient for this to be clinically appropriate, referral to drug treatment services should be considered as an alternative to arrest for those who are willing to engage with these services and can demonstrate consistent attendance. This is already done by several police forces.

Courts should consider increasing the use of Drug Rehabilitation Requirements with or without Mental Health Treatment Requirements within community sentences for offenders with drug use disorders involving synthetic cathinones who have been assessed as suitable (because of regular drug use associated with dependency) and who consent to this approach.

Following on from previous advice (recommendation 2) provided by the ACMD 'Custody-community transitions' report (ACMD 2019c), it remains important to reduce the proportion of people who leave prison with unsettled or unknown accommodation on the first night of release and increase the proportion of people who have an assessed need for drug treatment on release who enter treatment in the community within 4 weeks of release.

Leads: Home Office; police forces; courts; prison services.

Measure of outcome: Establishment of support programmes in police stations. Increased referral to drug treatment services from the police. Increased numbers of community sentences with Drug Rehabilitation Requirements involving synthetic cathinone users.

RECOMMENDATION 6: The government should establish an appropriately managed fund, possibly within the 'Safer Streets' initiative, to support local policing and/or public health initiatives in communities that are particularly affected by drug use.

Adequate resourcing is needed to support local policing initiatives in communities affected by drug use, with the aim of protecting and reassuring local people. The precise measures needed, and the resource required, should be considered locally, but might include fixed resources such as additional CCTV and street lighting. It may also be useful for funds to be available to support local public health initiatives aimed at reducing harms associated with drugs in areas where prevalence is particularly high.

Police and Crime Commissioners have already had the opportunity to bid for resources via the Safer Streets fund launched in 2023. The extension of this fund or the establishment of a further fund to support local initiatives in communities affected by drug use should be considered, not just for fixed infrastructure but potentially also for additional surveillance and, where justified, the employment of staff. This initiative should not be confined to areas affected by synthetic cathinone use, but also those affected by other illicit drugs.

Leads: Home Office; Police, Fire and Crime Commissioners; OHID; local authorities and equivalents in devolved administrations.

Measure of outcome: Establishment of an appropriate fund and distribution to affected communities.

Education and training

RECOMMENDATION 7: More detailed information on the effects of synthetic cathinones should be made available to people who use drugs, the public and staff who may encounter drug users, including those working in health, social care housing and criminal justice settings.

The public facing website Frank already contains information on synthetic cathinones, including reference to 'monkey dust'. This information should be updated to include information on the content of 'monkey dust' preparations and more detailed information on cathinones other than mephedrone, including potential adverse effects of pyrrolidino-cathinones. Information should also be provided in an appropriate format for younger people and for those engaging in chemsex. This information should also be provided by other information sources, including the DAN 24/7 telephone helpline in Wales.

Health professionals can register to access information and clinical management advice about potentially toxic substances, including illicit drugs, via the TOXBASE® website. Currently, a search for 'monkey dust' on TOXBASE® takes the user to a general page on unknown drugs of misuse. This should be updated to provide more specific information on the contents of 'monkey dust' preparations. Information should also be provided on MDPHP, which currently does not appear to have a specific entry on the website.

Employing organisations such as NHS Trusts and Boards, local authorities and the police should review training provided for staff who may come into contact with people who use drugs. They should ensure that this includes information on the drugs that are commonly used in their local area, the active constituents of street drug products (such as 'monkey dust') and their potential adverse health effects. They should also be familiar with appropriate referral pathways and management of people who use drugs. Training should be designed to reduce stigmatising attitudes of staff towards people who use drugs, including those who use synthetic cathinones. Training should be reviewed regularly and updated to include new and locally emerging substances.

This advice builds on advice about staff training (Recommendation 2) provided in the earlier ACMD report *'*Ageing cohort of drug users' (ACMD, 2019b).

Leads: Talk to Frank website; Dan 24/7; National Poisons Information Service; UK Health Security Agency; NHS Trusts and Boards; local authorities and their devolved equivalents; police forces.

Measure of outcome: Availability of appropriate online information. Delivery of updated information and training by responsible agencies.

Monitoring, surveillance and research

RECOMMENDATION 8: More detailed and regular analysis of the contents of 'monkey dust' and other commonly encountered NPS preparations should be carried out to monitor their contents and, when possible, purity.

Currently, there is limited information available on the contents of 'monkey dust' preparations in circulation. Police forces in affected areas should establish a programme of regular and systematic analysis of seized 'monkey dust' preparations to track their contents and, when possible, purity. Resource should be made available to allow this to happen.

Leads: Home Office; police forces in affected areas.

Measure of outcome: Reporting the content of seized 'monkey dust' preparations at least annually.

RECOMMENDATION 9: The development of improved field testing of street drugs, including 'monkey dust' preparations, should be funded with the aim of detecting different synthetic cathinones.

It would be helpful to police forces to have methods of field testing available that can identify synthetic cathinones in seized materials and differentiate them from other illicit drugs. Materials containing synthetic cathinones could then be sent for more detailed forensic analysis to identify the specific compounds involved. This would be a more cost-efficient approach than sending all samples for detailed analysis. It would facilitate criminal prosecution of offenders and the identification of those needing drug treatment and rehabilitation in relation to synthetic cathinone use. It would also provide more detailed analytical information, so that problem compounds and patterns of use could be identified at an earlier stage.

Funding should be provided to develop improved field testing of illicit drug product including "monkey dust" preparations, to detect different synthetic cathinones. This should align appropriately with Evidential Drug Identification Testing (EDIT) and testing for public and social health purposes. This could involve development of a simple colour tests using the Marquis Reagent described in paragraph 16.12.

Leads: Home Office; National Police Chief's Council; police forces in affected areas.

Measure of outcome: Development and roll out of an effective field-testing methodology to identify synthetic cathinones.

RECOMMENDATION 10: Research should be funded to study the appropriate management of stimulant use disorders including those associated with synthetic cathinones.

There is currently some uncertainty about the optimum management and effectiveness of drug use disorders involving stimulants, including synthetic cathinones, including the role of talking therapies.

Research funding organisations such as the National Institute for Health and Care Research (NIHR) should consider this area for funding, possibly via the Health Technology Assessment (HTA) programme.

Leads: NIHR; HTA Programme

Measure of outcome: Inclusion in the HTA funding programme or an alternative.

RECOMMENDATION 11: Research should be undertaken to compare the pharmacology and human health harms of individual cathinones that are currently prevalent in the UK.

This review has identified evidence gaps that have made it difficult to make robust comparisons between the pharmacology of different stimulants, including different types of synthetic cathinone. There is also a lack of comparative information on the adverse human health effects of these compounds, including their acute toxicity and their ability to induce drug dependence.

It would be useful to develop expertise and research capacity within the UK for the study of the pharmacology and human health effects of different stimulants, including those that may emerge in the future. Research on the relationship between findings in animal studies and effects in humans is also required.

UK funding bodies such as the Medical Research Council (MRC) and NIHR should consider these areas of research for future funding.

Leads: MRC; NIHR.

Measure of outcome: Availability of research funding.

RECOMMENDATION 12: Research should be funded to better understand the reasons for the high prevalence of use of pyrrolidino-cathinones in North Staffordshire and its environs.

Evidence obtained for this review has demonstrated that use of pyrrolidino-cathinones, especially as constituents of ‘monkey dust’, is highly concentrated in North Staffordshire and its environs. The reason for this is unclear and it would be useful to have information about this in order to better plan appropriate responses in areas affected and elsewhere.

Local authorities and police forces should consider funding research to better understand the underlying reasons for the increased use of synthetic cathinones in areas of high prevalence.

Leads: Local authorities and police forces in areas of high prevalence.

Measure of outcome: Local availability of research funding.

RECOMMENDATION 13: In the event of changes being made to the legal status of synthetic cathinones, research should be funded to examine the impact of these changes on their availability and on health and social harms associated with these and related compounds in the UK.

There is currently little information available on the impact of different levels of legal control on the health and social harms of drugs of misuse. As a result, there remains uncertainty about the effects of increasing the level of classification for compounds already controlled via the MDA.

Should such a change be enacted now or in the future, research should be conducted to examine the impact of this on the availability of these and related compounds and on drug-related health and social harms. This should include monitoring related drug seizures and human health harms including drug-related deaths. This research should not be restricted to synthetic cathinones as there is a need to monitor for the possible displacement towards other related compounds, such as amphetamines and cocaine.

Lead: Home Office

Measure of outcome: Publication of a review of the impact of legal changes within 5 years of implementation of any change in legislation.

RECOMMENDATION 14: Government should discuss developing a closer working relationship with the European Union Drugs Agency to facilitate better sharing of information about illicit substances in circulation in the EU and UK.

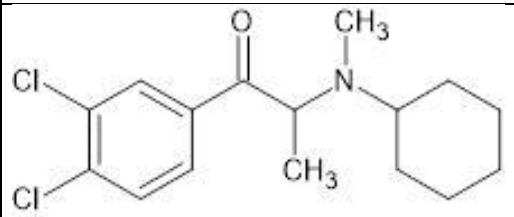
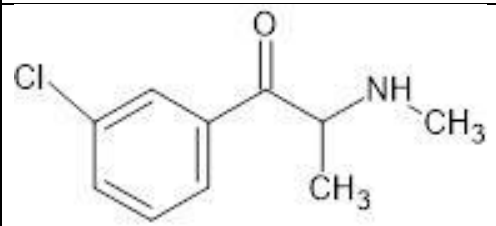
The current lack of joint working between the UK and EU in the area of drug misuse is a significant disadvantage to both sides, as it has resulted in a loss of data sharing and the need to duplicate work of mutual importance. Drafting this report, for example, has been made more difficult and time consuming due to lack of access to resources held by EUDA, including the ENDD. This restricts the information available to UK stakeholders about drugs in circulation within the EU. This is an important disadvantage because of the high risk that these substances may also appear here. Work to establish the chemistry, pharmacology, and health harms of drugs of misuse and especially NPS would be greatly assisted by access to the resources already held on the ENDD, which the UK no longer has access to.

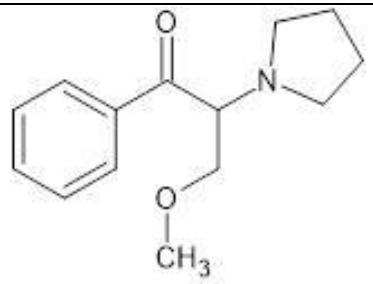
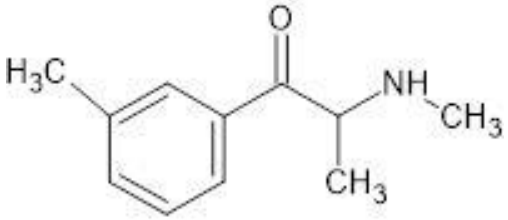
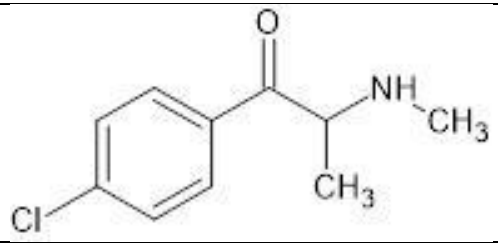
There would be significant mutual advantages to the negotiation of a memorandum of understanding to underpin joint working on drug issues and access to information held by each side.

Lead: UK government.

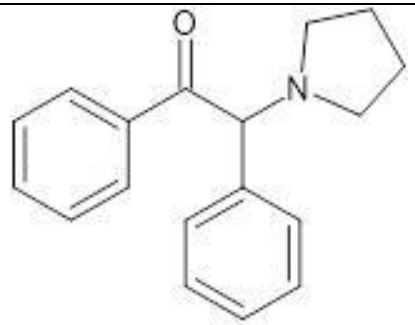
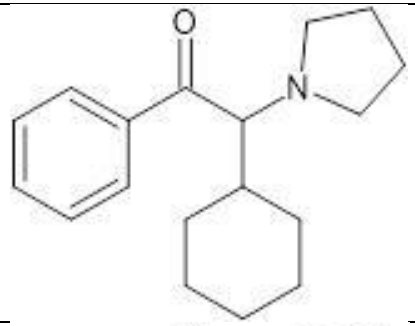
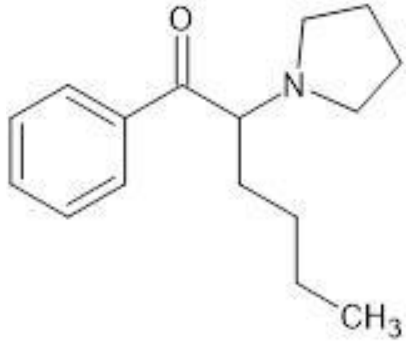
Measure of outcome: Establishment of a formal working arrangement between the UK and EUDA.

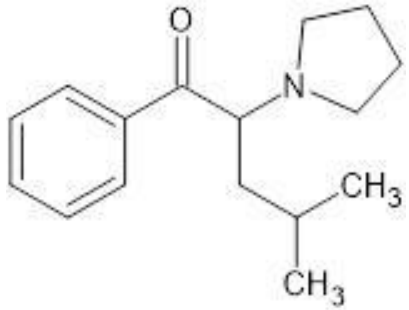
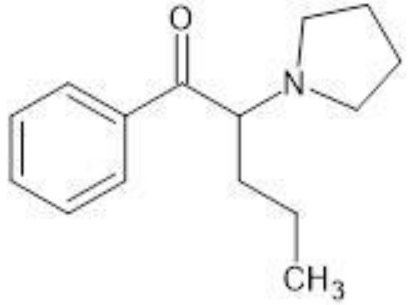
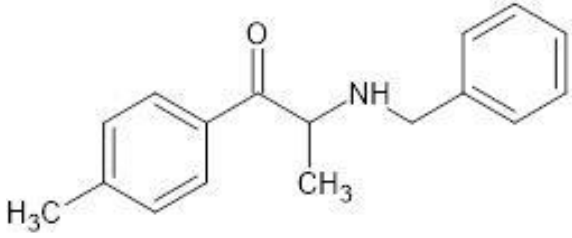
Annex A: Names, synonyms and abbreviations used for compounds discussed in this report

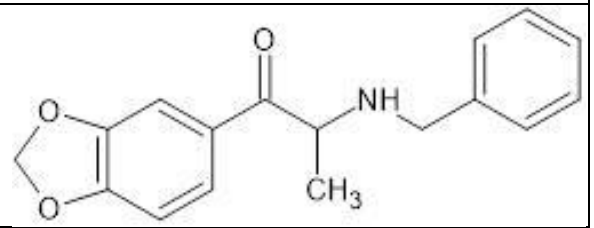
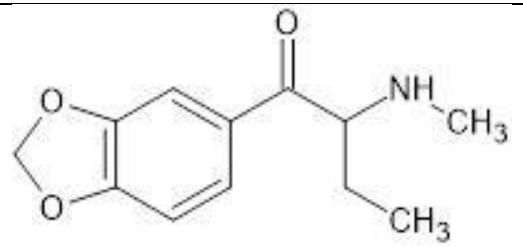
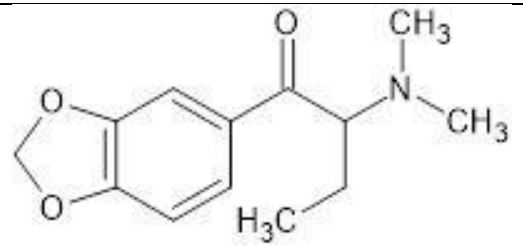
Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
2,4-DMEC	2,4-Dimethylethcathinone	1-(2,4-Dimethylphenyl)-2-methylamino-propan-1-one	
2-MMC	2-Methylmethcathinone	1-(2-Methylphenyl)-2-methylamino-propan-1-one	
3,4-dichloro-*N*-methyl-*N*-cyclohexylcathinone*	3,4-DCCHMC	1-(3,4-dichlorophenyl)-2-(cyclohexyl(methyl)amino)propan-1-one	
3-CEC	3-Chloroethcathinone	1-(3-Chlorophenyl)-2-ethylamino-propan-1-one	
3-CMC	3-Chloromethcathinone	1-(3-Chlorophenyl)-2-methylamino-propan-1-one	
3-FMC	3-Fluoromethcathinone	1-(3-Fluorophenyl)-2-methylamino-propan-1-one	
3-MEC	3-Methylethcathinone	1-(3-Methylphenyl)-2-ethylamino-propan-1-one	

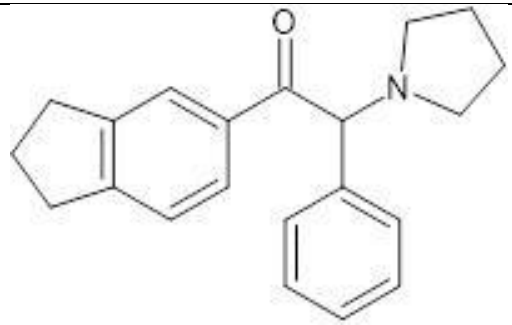
Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
3-Methoxy-α-PPP*	3-Methoxy-α-Pyrrolidinopropiophenone, α-PPP-3-MeO	1-Phenyl-2-(pyrrolidin-1-yl)-3-methoxypropan-1-one	
3-MMC	3-Methylmethcathinone	1-(3-Methylphenyl)-2-methylamino-propan-1-one	
4-CDMC	4-Cl-N, *N*-Dimethylcathinone	1-(4-Chlorophenyl)-2-dimethylamino-propan-1-one	
4-CEC	4-Chloroethcathinone	1-(4-Chlorophenyl)-2-ethylamino-propan-1-one	
4-Cl-EMC	4-chloropentedrone	1-(4-Chlorophenyl)-2-methylamino)-pentan-1-one	
4-Cl-α-PPP	4-Chloro-α-pyrrolidinopropiophenone	1-(4-Chlorophenyl)-2-pyrrolidin-1-yl-propan-1-one	
4-Cl-α-PVP	4-Chloro-α-pyrrolidinovalerophenone	1-(4-Chlorophenyl)-2-pyrrolidin-1-yl-pentan-1-one	
4-CMC	4-Chloromethcathinone, Clephedrone	1-(4-Chlorophenyl)-2-methylamino-propan-1-one	

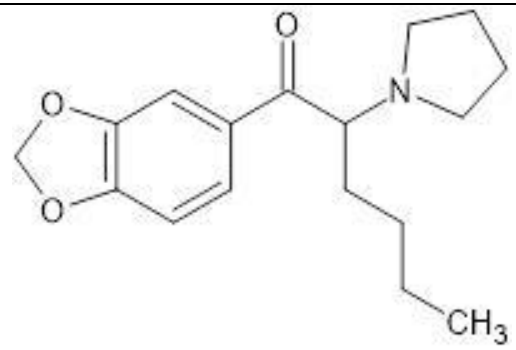
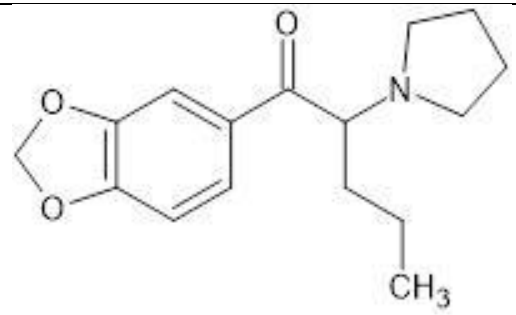
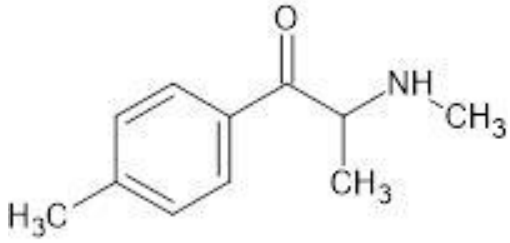
Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
4-EMC	4-Ethylmethcathinone	1-(4-Ethylphenyl)-2-methylamino-propan-1-one	
4F-3-Methyl-α-PVP	4-Fluoro-3-methyl- α-pyrrolidinovalerophenone	1-(4-Fluoro-3-Methyl-phenyl)-2-(pyrrolidin-1-yl)-pentan-1-one	
4F-3-Methyl-α-PHP	4-Fluoro-3-Methyl-α-pyrrolidinohexiophenone	1-(3-Methyl-4-fluorophenyl)-2-pyrrolidin-1-yl-hexan-1-one	
4-Fluoropentedrone		1-(4-Fluorophenyl)-2-methylamino-pentan-1-one	
4F-PV8	4-Fluoro α-PHPP, 4'-fluoro-α-pyrrolidinoheptophenone, 4F-α -PEP	1-(4-Fluorophenyl)-2-pyrrolidin-1-yl-heptan-1-one	
4F-α-PiHP	4-Fluoro-α-pyrrolidinoisohexanophenone	1-(4-Fluorophenyl)-2-pyrrolidin-1-yl-4-methylpentan-1-one	
4F-α-PHP	4-Fluoro-α-pyrrolidinohexiophenone	1-(4-Fluorophenyl)-2-pyrrolidin-1-yl-hexan-1-one	
4F-α-PVP	4-Fluoro-α-pyrrolidinovalerophenone,	1-(4-Fluorophenyl)-2-pyrrolidin-1-yl-pentan-1-one	
4-MEC	4-Methylethcathinone	1-(4-Methylphenyl)-2-(ethylamino)-propan-1-one	
4-methyl buphedrone, *N*-benzyl derivative*		1-(4-methylphenyl)-2-benzylamino-butan-1-one	
4-MP	4-Methylpentedrone	1-(4-Methylphenyl)-2-methylamino-pentan-1-one	
4-Methylpentylone	Isohexylone	1-(MDO-phenyl)-2-methylamino-4-methylpentan-1-one	
4-MPHP	4'-Methyl-α-pyrrolidinohexiophenone	1-(4-Methylphenyl)-2-pyrrolidin-1-yl-hexan-1-one	

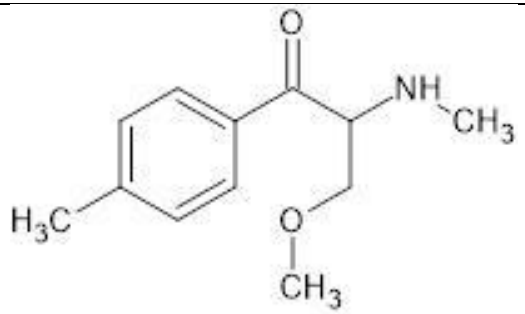
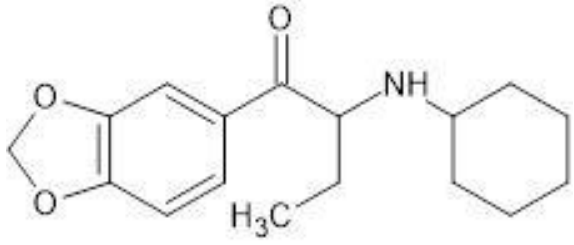
Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
α-D2PV*	α-Pyrrolidino-2-phenylacetophenone, DPPE	1-Phenyl-2-pyrrolidin-1-yl-2-phenyl-ethan-1-one*	
α-PBP	α-Pyrrolidinobutiophenone	1-Phenyl-2-pyrrolidin-1-yl-butan-1-one	
α-PCyP*	α-Pyrrolidinocyclohexylphenone	1-phenyl-2-(pyrrolidin-1-yl)-2-cyclohexyl-ethan-1-one	
α-PHP	α-Pyrrolidinohexiophenone	1-Phenyl-2-pyrrolidin-1-yl-hexan-1-one	

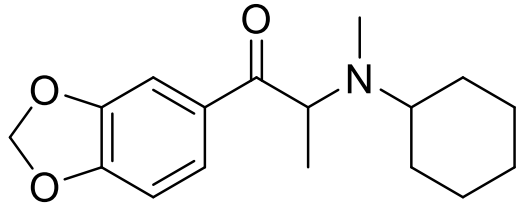
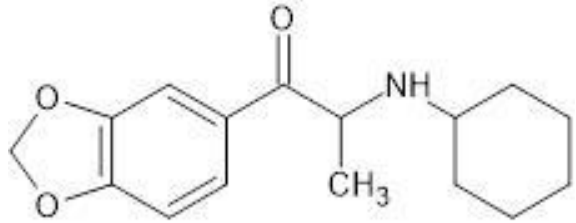
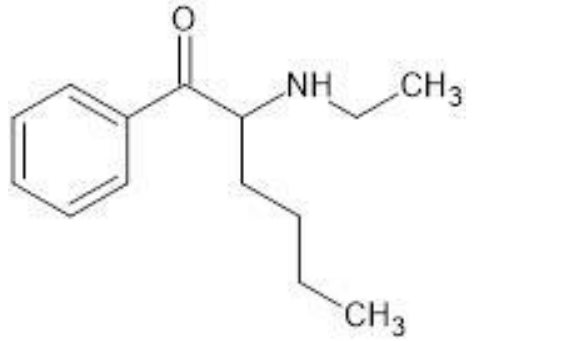
Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
α-PiHP	α-Pyrrolidinoisohexanophenone	1-Phenyl-2-pyrrolidin-1-yl-4-methylpentan-1-one	
α-PVP	α-Pyrrolidinovalerophenone	1-Phenyl-2-pyrrolidin-1-yl-pentan-1-one	
α-PNP	α-pyrrolidinononaphenone	1-Phenyl-2-pyrrolidin-1-yl-nonan-1-one	
Benzedrone*	4-Methyl-*N*-benzylcathinone, 4-MBC	1-(4-Methylphenyl)-2-benzylamino-propan-1-one	
BMDB*		1-(3,4-methylenedioxyphenyl)-2-benzylamino-propan-1-one	

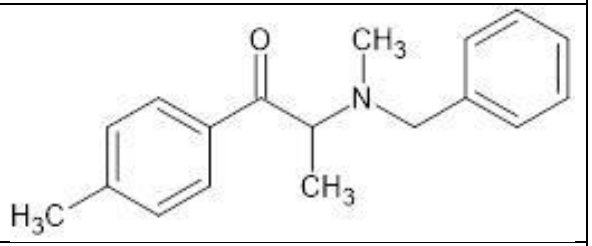
Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
BMDP*	3,4-Methylenedioxy-*N*-benzylcathinone, Benzylone	1-(3,4-MDO-phenyl)-2-benzylamino-propan-1-one	
Brephedrone	4-Bromomethcathinone (4-BMC)	1-(4-Bromophenyl)-2-methylamino-butan-1-one	
Buphedrone	α-methylamino-butyrophenone (MABP)	1-Phenyl-2-methylamino-butan-1-one	
Butylone	β-keto-*N*-methylbenzodioxolylbutanamine (βk-MBDB)	1-(3,4-MDO-phenyl)-2-methylamino-butan-1-one	
CEC (not specified)	See 3- or 4-CEC		
CMC (not specified)	See 3- or 4-CMC		
Dibutylone	βk-DMBDB, βk-Methyl-K	1-(3,4-MDO-phenyl)-2-dimethylamino-butan-1-one	
Dimethylone	β-keto-methylenedioxydimethylamphetamine (βk-MDDMA)	1-(3,4-MDO-phenyl)-2-dimethylamino-propan-1-one	
Dipentylone	Dimethylpentylone, *N*-*N*-dimethylpentylone	1-(3,4-MDO-phenyl)-2-dimethylamino-pentan-1-one	
EMC (not specified)	See 3-EMC		

Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
Ephedrone	Methcathinone	1-Phenyl-2-methylamino-propan-1-one	
Ephylone	*N*-Ethylpentylone, *N*-Ethylnorpentylone, βk-EBDP	1-(3,4-MDO-phenyl)-2-ethylamino-pentan-1-one	
Ethcathinone	*N*-Ethylcathinone	1-Phenyl-2-ethylamino-propan-1-one	
Eutylone	β-keto-1,3-benzodioxolyl-*N*-ethylbutanamine, βk-EBDB	1-(3,4-MDO-phenyl)-2-ethylamino-butan-1-one	
Flephedrone	4-Fluoromethcathinone (4-FMC)	1-(4-Fluorophenyl)-2-methylamino-propan-1-one	
Indapyrophenidone*		1-(2,3-dihydro-1H-inden-5-yl)-2-pyrrolidin-1-yl)-2-phenyl-ethan-1-one	
MDO-PPP	methylenedioxy-α-pyrrolidinopropiophenone, MDPPP	1-(MDO-phenyl)-2-pyrrolidino-propan-1-one	
3',4'-Methylenedioxy-α-methyl-PPP		1-(MDO-phenyl)-2-pyrrolidin-1-yl-2-methyl-propan-1-one	
MDPBP	3',4'-Methylenedioxy-α-pyrrolidinobutyrophenone	1-(3,4-MDO-phenyl)-2-pyrrolidin-1-yl-butan-1-one	
MDPEP	MD-PV8, MDPHPP	1-(3,4-MDO-phenyl)-2-(pyrrolidin-1-yl)-heptan-1-one	

Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
MDPHP	3',4'-Methylenedioxy-α-pyrrolidinohexiophenone	1-(3,4-MDO-phenyl)-2-pyrrolidin-1-yl-hexan-1-one	
MDPV	Methylenedioxypyrovalerone	1-(3,4-MDO-phenyl)-2-pyrrolidin-1-yl-pentan-1-one	
MEC (not specified)	See 3- or 4-MEC		
Mephedrone	4-Methylmethcathinone (4-MMC), MCAT	1-(4-Methylphenyl)-2-methylamino-propan-1-one	
Metamfepramone	*N*,*N*-Dimethylcathinone	1-Phenyl-2-(dimethylamino)-propan-1-one	
Methedrone	Para-methoxymethcathinone, 4-methoxymethcathinone, βk-PMMA, PMMC, methoxyphedrine, 4-MeOMC	1-(4-Methoxyphenyl)-2-methylamino-propan-1-one	

Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
4-MEAP	4-Methyl-α-ethylaminopentiophenone, 4-Methyl-*N*-ethylnorpentedrone	1-(4-methylphenyl)-2-(ethylamino)-pentan-1-one	
Methylone	3,4-Methylenedioxy-*N*-methylcathinone, MDMC	3,4-methylenedioxy-N-methylcathinone (MDMC)	
Mexedrone*	4-MMC-MeO	1-(4-Methylphenyl)-2-methylamino-3-methoxypropan-1-one	
MMC (not specified)	See 2- or 3- or 4-MMC		
MPBP	4'-Methyl-α-pyrrolidinobutiophenone	1-(4-Methylphenyl)-2-pyrrolidin-1-yl-butan-1-one	
Naphyrone	O-2482, Naphthylpyrovalerone	1-(Naphth-2-yl)-2-pyrrolidin-1-yl-pentan-1-one	
N-Butylhexedrone	α-Butylaminohexanophenone	1-Phenyl-2-butylamino-hexan-1-one	
N-Butylpentylone	βk-BBDP, βk-Butyl-K	1-(3,4-MDO-phenyl)-2-butylamino-pentan-1-one	
N-Cyclohexylnorbutylone*		1-(3,4-MDO-phenyl)-2-(cyclohexylamino)-butan-1-one	

Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
N-Cyclohexylmethylone*		1-(3,4-MDO-phenyl)-2(cyclohexyl(methyl)amino)-propan-1-one	
N-Cyclohexylnormethylone*	Cyputylone	1-(3,4-MDO-phenyl)-2-cyclohexylamino-propan-1-one	
N-Ethylheptedrone		1-Phenyl-2-ethylamino-heptan-1-one	
N-Ethylhexedrone		1-Phenyl-2-ethylamino-hexan-1-one	
N-Ethylhexylone		1-(3,4-MDO-phenyl)-2-ethylamino-hexan-1-one	
N-Ethylpentedrone	NEP, *N*-ethylnorpentedrone, α-Ethylaminopentiophenone	1-phenyl-2-ethylamino-pentan-1-one	
N-Ethylbuphedrone	NEB	1-Phenyl-2-ethylamino-butan-1-one	
NiPP	*N*-Isopropylpentedrone	1-Phenyl-2-(isopropylamino)-pentan-1-one	

Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
N-Methylbenzedrone*	*N*-Methyl-4-MBC	1-(4-methylphenyl)- 2-[methyl(benzyl)amino]-propan-1-one	
4-Methyl buphedrone, *N*-benzyl derivative*		1-(4-Methylphenyl)-2-benzylamino-butan-1-one	
N-methyl-bk-MMDA-2		1-(3,4-MDO-6-methoxy-phenyl)-2-methylamino-propan-1-one	
N-Methylmethedrone	4-Methoxy-*N*, *N*-dimethylcathinone	1-(4-Methylphenyl)- 2-dimethylamino-propan-1-one	
Normephedrone	4-Methylcathinone	1-(4-Methylphenyl)-2-amino-propan-1-one	
N-Propylbutylone	β-keto-*N*-Propyl-1-(1,3-benzodioxol-5-yl)-butanamine, βk-PBDB, Putylone	3,4-MDO-phenyl)-2-(propylamino)butan-1-one	
N-Propylnorpentedrone		1-Phenyl-2-(propylamino)-pentan-1-one	
Pentedrone	α-Methylaminovalerophenone, β-ethylmethcathinone, β-EMC	1-phenyl-2-methylamino-pentan-1-one	
Pentylone	βk-MBDP	1-(3,4-MDO-phenyl)-2-methylamino-pentan-1-one	
Propylone	3,4-Methylenedioxy-*N*-propylcathinone, Propyl-3,4-methylenedioxy-cathinone	1-(3,4-MDO-phenyl)-2-propylamino-propan-1-one	
Pyrovalerone	4-Methyl-β-keto-prolintane	1-(4-Methylphenyl)-2-pyrrolidin-1-yl-pentan-1-one	
Tertylone	3',4'-Methylenedioxy-*N*-tert-butylcathinone, 3,4-MDO-*N*-tBu-cathinone, MDPT, tBuONE	1-(3,4-MDO-phenyl)-2-(tert-butylamino)-propan-1-one	

Common name or abbreviation	Synonyms	Structure (in form: 1-(ring structure)-2-(amine structure)-alkyl ketone)	Drawn structure (selected compounds only)
TH-PVP	3',4'-Tetramethylene-α-Pyrrolidinovalerophenone (Tetralin version of MDPV)	1-(Tetralin-6-yl)-2-pyrrolidin-1-yl-pentan-1-one	

Annex B: International legislative control of synthetic cathinones

Three cathinones had been placed under international control prior to 2015 and are named in the list of materials covered by the 1971 United Nations Convention on Psychotropic Substances (the 'Green List'). Cathinone (Schedule I, most restrictive) and pyrovalerone (Schedule IV, least restrictive) had been listed in 1986 and methcathinone (Schedule I) in 1995.

Since 2015, following the emergence of cathinones as NPS and increasing evidence of their harms, 16 further cathinones have been added to Schedule II of the Green List to bring the total to 19 by 2024 (see Table 8 for details).

All nations which are signatories to the UN Drug Conventions are obliged to control listed materials by means of their national legislation, with the level of control reflecting their UN scheduling.

Table 8. Cathinones listed within 1971 UN Convention on Psychotropic Substances (the 'Green List'), their schedule within that convention and the year when added

Material	Schedule	Year
Cathinone	I	1986
Pyrovalerone	IV	1986
Methcathinone	I	1995
Mephedrone	II	2015
MDPV	II	2015
Methylone	II	2015
α-PVP	II	2016
4-MEC	II	2017
Ethylone	II	2017
Pentedrone	II	2017
Ephylone	II	2019
4-CMC	II	2020
N-Ethylhexedrone	II	2020
α-PHP	II	2020
Eutylone	II	2022
α-PiHP	II	2023
3-MMC	II	2023
3-CMC	II	2024
Dipentylone	II	2024

European controls

The EU, which operates a system to monitor and assess the harms of NPS within Europe, also requires its member states to control certain additional cathinones. Although the EU's list of specified substances closely resembles that of the UN, EU

action can occasionally precede the UN's; for example, mephedrone was placed under EU-wide control in 2010 but only became UN-listed in 2015.

National controls

As the number of cathinone NPSs identified has continued to expand, many countries have chosen to control other named cathinones beyond those in the UN's list. In addition, as the number of cathinone NPSs has increased, some countries have adopted strategies to control groups of cathinones without having to individually list the chemicals. Several have enacted broad generic (structure-based) controls to cover numbers of substances, similar to that used in the UK, including Germany, France, Norway, Japan and Switzerland.

The level of control applied to different cathinone NPS within a nation's legislation tends to be standard across materials, rather than particular substances being subject to different levels of control. The only exceptions to this are materials with accepted medical applications, such as pyrovalerone, diethylpropion and bupropion, which have been allocated lower levels of control.

Some examples of controls on cathinones introduced by other countries are described below.

Germany

In the German BtMG (Narcotic Act), 13 cathinones are named in Annex I (non-tradeable narcotics) and a further 21 in Annex II (non-prescription narcotics). In addition, the NpSG (New Psychoactive Substances Act) includes an extremely broad generic control on cathinones.

France

The French 'List of Substances Classed as Stupifiants' includes a limited number of named cathinones in Annex III while in Annex IV there are 2 generic controls, one covering derivatives of cathinone and the other covering derivatives of cathinones where the phenyl ring is replaced by other monocyclic and polycyclic systems. Interestingly, the list of examples of materials cited as being covered by the generics includes benzedrone and 2 "iso-cathinones", where the position of the carbonyl and amine groups are reversed, and which would therefore appear to be outside the scope of the current UK generic.

Netherlands

Holland's Opium Act includes 2 lists of individually specified controlled drugs, List 1 and 2. This was amended in 2024 by the addition of a new "List 1A" which includes several generic controls on NPS 'families', including one addressing cathinones, using wording very similar to the UK's generic. This measure will align which materials are controlled with neighbouring countries, including the UK.

Switzerland

In the lists of materials controlled in Switzerland, several named cathinones appear in Annexes 1 and 5, while Annex 6 includes 2 generic controls, one addressing

cathinone variants and the other variants where the phenyl ring has been replaced by any other monocyclic or polycyclic structure.

Japan

Japan's list of controlled substances includes 17 named cathinones, while its list of 'Designated Substances' (NPS) lists around 25 further materials and includes as Item #326 a generic control which is claimed to cover 1,331 substances.

China

China had been regarded as the major source for NPS entering the UK. However, since 2015 Chinese legislative control has been progressively expanded to address many NPS in addition to those under international control, including cathinones. For example, the MDPV homologues MDPPP and MDPBP were controlled in China in September 2015 and MDPHP in August 2018. There are now some 60 individually named cathinones within the Chinese controls. The most recent tranche of 7 cathinones which were brought under Chinese control in July 2024 includes α-PiHP, dipentylone, 4F-3-Me-α-PVP and *N*-cyclohexylnormethylone, all materials which are considered within this report (MPS, 2024). Recent indications are that production of cathinones for the European market has switched away from China to India, Eastern Europe and, to a degree, the Netherlands.

USA

The US Controlled Substances Act includes several named cathinones as Schedule 1 materials. Although there is no generic control of cathinones, controls also cover "positional isomers", defined as any rearrangement of structural units within a molecule which retains chemical functionality. This means, for example, that the control of mephedrone (4-MMC) not only covers 2- and 3-MMC, but also buphedrone, ethcathinone and *N,N*-dimethylcathinone as these are cathinones with the same molecular formula. Similarly, the control of MDPV is taken to also control N-cyclohexylnormethylone.

Annex C: UK stakeholder responses

ACMD wrote seeking quantitative information about synthetic cathinones from a range of stakeholders in April 2024. These included public health authorities, forensic service providers and research studies. Their responses are detailed below.

Submitted sample analysis

WEDINOS

The Welsh Emerging Drugs and Identification of Novel Substances Project (WEDINOS) analyses samples of drug samples submitted anonymously by users from across the UK. The numbers of identifications of synthetic cathinones within samples submitted to WEDINOS for the period 2019-2023 are shown in Table 9.

Mephedrone and 4-CMC were the synthetic cathinones most detected. There were no reported detections of MDPHP, but α-PHP and α-PVP were identified in some samples. Mexedrone and α-D2PV, compounds that are not currently captured by the generic text in the MDA, were also identified in a few samples. Overall, the largest numbers of detections were made from samples received in 2021.

Table 9. Numbers of samples submitted to the WEDINOS study containing synthetic cathinones, 2019 to 2023

Synthetic cathinone	2019	2020	2021	2022	2023	Total
Mephedrone	35	47	55	61	74	272
4-CMC	4	4	63	31	27	129
3-MMC	2	6	20	8	9	45
Dipentylone	0	0	0	14	6	20
Eutylone	0	7	2	10	1	20
4-CEC	7	3	3	1	0	14
N-ethylheptedrone	5	4	5	0	0	14
α-PHP	0	2	2	5	2	11
α-PVP	0	1	3	4	2	10
Mexedrone*	3	2	3	0	0	8
4F-3-methyl-α-PVP	0	2	3	0	2	7
Dibutylone	0	0	6	0	0	6
Ephylone	3	0	1	0	0	4
N-ethylhexedrone	1	3	0	0	0	4
Normethylone	1	2	0	0	0	3
4-MEAP	1	1	1	0	0	3
Methylone	1	0	0	1	1	3
MPBP	0	0	1	1	0	2
N-butylhexedrone	0	0	2	0	0	2
N-ethylpentedrone	0	0	1	1	0	2

Synthetic cathinone	2019	2020	2021	2022	2023	Total
2-MMC	0	0	0	0	1	1
4F-3-methyl-α-PHP	0	0	1	0	0	1
α-D2PV*	0	0	1	0	0	1
Ethylone	0	0	0	0	1	1
N-butylpentylone	0	0	0	0	1	1
Pentedrone	0	1	0	0	0	1
Pentylone	0	1	0	0	0	1
TOTAL	**63**	**86**	**173**	**137**	**127**	**586**

*Compounds not covered by current generic text in the MDA.

TICTAC

TICTAC Communications Ltd provided data from analysis of drugs either seized, or voluntarily placed in amnesty bins at 13 UK festivals, with analysis performed using gas chromatography mass spectroscopy (GC-MS) and Fourier Transfer Infrared spectrometry (FTIR). Drugs from one festival for which there were high numbers of cathinone detections in 2021 and 2022 were not analysed for 2023 and this may contribute to lower numbers of detections in that year. However, numbers were also reduced in 2023 for the festivals that were studied over all 3 of these years. The most common compounds detected over the 4 years were 3- or 4-CMC, mephedrone and ethylone (Table 10). Of note, MDPHP has not been detected in this survey since 2018.

Table 10. Detections of synthetic cathinones at UK festivals, 2019 to 2023 (no festivals held during 2020)

Synthetic cathinone	2019	2021	2022	2023	Total
3- or 4-CMC[1]	0	69	22	3	94
4-CMC	0	9	34	8	51
Mephedrone	10	25	11	0	46
Ethylone	3	18	1	0	22
Ephylone	6	14	0	0	20
Dipentylone	0	4	13	0	17
3-CMC	0	6	8	0	14
3-MMC	0	0	10	0	10
3- or 4-MMC[1]	0	7	0	1	8
4F-3-methyl-α-PVP	0	8	0	0	8
Methylone	2	0	0	0	2
BMDP	0	1	0	0	1
α-PHP	0	1	0	0	1
Mexedrone	1	0	0	0	1
Pentylone	0	1	0	0	1
Drug combinations					
3- or 4-CMC[1] and 3- or 4-CEC[1]	0	3	0	0	3

Synthetic cathinone	2019	2021	2022	2023	Total
4-MMC and 4-CMC	0	0	2	0	2
TOTAL	**22**	**166**	**101**	**12**	**301**

[1]Isomers not distinguishable using GC-MS

Drug seizures

The annual number of mephedrone seizures made by law enforcement agencies in England and Wales peaked in year ending March 2013 and has subsequently fallen, with reductions in mephedrone seizures also reported from other devolved administrations over a similar time course (Corkery and others, 2018).

Office for Health Improvement and Disparities (OHID)

Data on numbers of drug seizures recorded by OHID are provided in Table 11.

Table 11. Detections of synthetic cathinones in drug seizures, as reported by OHID, 2017 to 2024

Synthetic cathinone	2017	2018	2019	2020	2021	2022	2023	2024*	Total
Mephedrone	46	33	69	64	126	79	125	29	571
Clephedrone	118	70	37	30	92	75	100	14	536
MDPHP	46	206	54	10	43	26	149	2	536
α-PHP	1		14	36	94	16	22		183
Ephylone	67	52	30	13	5	9	7		183
Mexedrone	63	39	15	11	4	1			133
Eutylone			2	14	57	22	8	1	104
α-PVP	35	11	7	3	1	11	2		70
α-PiHP	3	7	19	4	9	6	17	2	67
N-ethylhexedrone	18	16	8	7	4	1			54
4-chloro-α-PPP	26	8	9	3	1	2			49
4-Methyl-*N*-ethylnorpentedrone	28	10	4	2					44
Ethylone	17	8	1	2	4	3			35
BMDP*		3	7	3	16	1	2		32
Dibutylone	9	16	3	2	1	1			32
Dipentylone					1	3	22	4	30
3-MMC		1	3	9	6	1			20
4-MPHP	4	3	10		2				19
4-CDMC	3	3	5	5	2				18
4-Cl-α-PVP	8	6	2						16
N-methylbenzedrone*	9	5		1					15
MDPEP			4	10					14
4-MPD	7	3	2						12
2-MMC			2	1	3	3	1		10
4F-3-methyl-α-PHP					6	1		1	8

Synthetic cathinone	2017	2018	2019	2020	2021	2022	2023	2024*	Total
4F-α-PHP	2	5	1						8
4-MEC	2	3	1		2				8
Pentylone	1	1	1	1	1	3			8
MDO-PPP			1	1					2
3-CMC				1			1		2
4-EMC	1	1							2
4F-α-PVP				1		1			2
α-pyrrolidinononaphenone					2				2
Benzedrone						1	1		2
Butylone	1	1							2
MDPBP				1					1
4-chloropentedrone		1							1
4F-3-methyl-α-PVP					1				1
4-Fluoropentedrone					1				1
MPBP							1		1
Buphedrone	1								1
Metamfepramone	1								1
N-butylpentylone				1					1
N-ethylbuphedrone	1								1
N-ethylnorpentedrone		1							1
NiPP					1				1
Nor-mephedrone					1				1
N-propylnorpentedrone	1								1
TOTAL	**519**	**512**	**309**	**230**	**489**	**271**	**459**	**53**	**2,842**

*Data for Q1 (until March) 2024 only.

Eurofins Forensic Services

Eurofins Forensic Services laboratories provide a comprehensive forensic analysis service to police forces, legal and criminal justice organisations throughout the UK. Synthetic cathinones detected in seized samples for the period January 2019 to December 2023 (inclusive) are summarised in Table 12.

A total of 2,045 synthetic cathinone detections were reported, with the 4 compounds most commonly identified over the 5 years (and for 2023 alone) being mephedrone, MDPHP, 4-CMC and α-PVP. The annual numbers of synthetic cathinones detected increased year by year between 2019 and 2023.

MDPHP was detected in samples seized by police forces in the West Midlands, Staffordshire and West Mercia (but not other police forces) and a large proportion of these were seized during 2023.

There were small numbers of detections of synthetic cathinones outside the scope of the current MDA generics, most commonly mexedrone, but also α-D2PV, N-cyclohexyl butylone and N-cyclohexyl methylone.

Table 12. Synthetic cathinone detections in samples from police drug seizures, 2019 to 2023, as reported by Eurofins Forensic Services

Synthetic cathinone	Detections by year					
	2019	2020	2021	2022	2023	Total
Mephedrone	55	90	99	100	97	441
MDPHP		12	46	75	268	401
4-CMC		5	95	174	105	379
α-PHP	14	35	102	19	36	206
Eutylone		9	47	27	9	92
Dipentylone			11	13	32	56
4-CEC	29	16	3	6	1	55
α-PiHP		9	6	12	22	49
Ephylone		7	10	11	13	41
3-MMC	1	3	12	21	4	41
Mexedrone*	12	16	10	1		39
MDPEP	13	20	4			37
Ethylone	2	3	12	9	1	27
BMPD*	12	3	4	3	1	23
α-PVP	6		5	5	6	22
2-MMC	1	3	2	10	1	17
4-CDMC	4	9	2	1		16
MDPV	1		3	7	1	12
4-MEC	4		2	4	1	11
4-Cl-α-PPP	6	4	1			11
N-Butylhexedrone	8				1	9
4F-3-Methyl-α-PVP			1	2	5	8
4-F-α-PVP		5				5
Tertylone		2			2	4
N-butylpentylone	1				3	4
N-Propylbutylone			2	2		4
N-ethylpentedrone					3	3
α-D2PV*					3	3
TH-PVP		2			1	3
EMC (not specified)				3		3
N-cyclohexylnorbutylone*					2	2
N-cyclohexylnormethylone*					2	2
Propylone			1	1		2
4F-PHP				2		2
N-ethylheptedrone			1	1		2
Flephedrone				2		2
Dibutylone	1	1				2
Methylone				1		1
N-Ethylhexedrone			1			1
4-Fluoropentedrone			1			1
4-MPHP			1			1
Pentylone			1			1

Synthetic cathinone	Detections by year					
	2019	2020	2021	2022	2023	Total
Bk-2C-B		1				1
N-Ethylhexylone	1					1
Dimethylone	1					1
4-methylpentylone	1					1
TOTAL	**173**	**255**	**485**	**512**	**620**	**2,045**

*Compounds not covered by current generic text.

The Emerging Drugs and Technologies Programme (EDAT)

The EDAT collates data from non-adopted seizures from UK Border Force hubs, which are transported to forensic service providers for analysis. It also purchases data on analyses of non-attributable samples from UK Prisons performed by TICTAC. Combined data from these 2 sources are shown in Table 13.

Methylmethcathinones (MMC), either mephedrone (4-MMC), 3-MMC, or MMC (unspecified) were commonly detected, with α -PHP, N-ethylhexedrone and 3-CMC or CMC (unspecified) also commonly identified. There were only 2 detections of MDPHP and only one of α-PVP. No materials outside the scope of the current MDA generics were identified (Table 13).

Table 13. Detections of synthetic cathinones in Border Force and UK prison samples, as reported by EDAT

Synthetic cathinone	2019/20	2020/21	2021/22	2022/23	2023/24	Total
MMC (not specified)			47		1	48
α-PHP		11	20	2	2	35
N-Ethylhexedrone		21	11			32
3-MMC		22		4		26
Mephedrone		13		5	2	20
3-CMC		15		4		19
CMC (not specified)		2	10		2	14
α-PiHP		9		2		11
Ethcathinone		5	4			9
N-Ethylpentedrone			1	3	1	5
2-MMC				4	1	5
4-MEC		1	2	1		4
Dipentylone				1	2	3
MDPHP			2			2
MDPEP		1				1
TH-PVP				1		1
Eutylone			1			1
4-Methylcathinone			1			1
4-CMC				1		1
4-CEC				1		1
3-MEC				1		1

Buphedrone				1		1
α-PVP	1					1
TOTAL	**1**	**100**	**100**	**30**	**11**	**242**

Note: Data are provided in financial years (April to March) by EDAT (formerly known as FEWS)

MANDRAKE

The Manchester Drug Analysis and Knowledge Exchange (MANDRAKE) project performs forensic/chemical analysis of seized samples using a variety of presumptive (FT-IR, IonScanner) and confirmatory (NMR and GC-MS) tests. The samples undergo qualitative and quantitative analysis (in triplicate, by GC-MS), using certified reference standards to confirm the purity of the seized samples.

The analysed samples were obtained from across Greater Manchester by Greater Manchester Police from the following sources: police seizures (property stores); night-time economy sources, including bars, nightclubs, and festivals; prison/custodial institutions and healthcare/drug treatment/coronial sources.

The most common substances identified were 4-CMC, mephedrone and MDPHP. BMDP and α-D2PV, both materials outside the scope of the current MDA generics, were also identified in a few samples. The purity of the analysed samples varied (Table 14). Most of the analysed samples were in the form of powders, but tablets containing mephedrone (234 mg/tablet), dipentylone (62-133 mg/tablet) and bk-PBDB (131mg to 136 mg per tablet, with caffeine 40mg to 43mg) were also submitted.

Table 14. Synthetic cathinones detected in samples from Greater Manchester analysed by MANDRAKE, 2019 to 2023

Synthetic cathinone	2019	2020	2021	2022	2023	TOTAL	Purity range
4-CMC	1	2	15	35	3	56	30-66%
Mephedrone	8	9	13	5	7	42	16-93%
MDPHP				14		14	21-99%
Dipentylone				5	1	6	-
BMDP*					5	5	7-26%
Ephylone	1	1		2	1	5	19-77%
3-CMC	1			1	1	3	67-93%
Eutylone					3	3	15-26%
3-MMC				2	1	3	60-69%
4F-3-methyl-α-PVP				2	1	3	93-96%
α-D2PV*					2	2	41-53%
α-PVP	1				1	2	71-83%
4F-α-PVP					1	1	81%
N-Propylbutylone				1		1	-

Synthetic cathinone	2019	2020	2021	2022	2023	TOTAL	Purity range
Ethylone					1	1	86%
TOTAL	**12**	**12**	**28**	**67**	**28**	**147**	

*Compounds not covered by current generic text.

Prison drug seizures, Scotland

The Scottish Prisons Non-Judicial Drug Monitoring Project is a collaboration between the Scottish Prison Service and the Leverhulme Research Centre for Forensic Science at the University of Dundee. The project tests drug seizures made across the Scottish prison estate in order to understand the drugs involved. Over the period April 2021 to October 2023 (inclusive), 6 samples, all analysed in 2023, were found to contain a synthetic cathinone, which was dipentylone in all 6 cases.

Forensic Service of Northern Ireland (FSNI)

FSNI provided data from toxicology analysis of bulk drug submissions analysed for the Police Service of Northern Ireland (PSNI) over the previous 5 years, as per their submission requests.

In the data they provided, mephedrone, ephylone and N-cyclohexyl methylone were the most commonly identified synthetic cathinones, with the latter outside the scope of the current MDA generic text. There were no detections of MDPHP (Table 15).

Table 15. Substances found in bulk drug submissions from Northern Ireland as analysed by FSNI, 2019 to 2023

Synthetic cathinone	2019	2020	2021	2022	2023	Total
Mephedrone	3	7	6	14	41	71
Ephylone	1		1	6	6	14
N-Cyclohexylnormethylone*				6	8	14
Ethcathinone					8	8
Methylone			4		4	8
Eutylone	1	1			2	4
4-CMC		1			1	2
4-CEC			1		1	2
α-PHiP			1		1	2
TOTAL	**5**	**9**	**13**	**26**	**72**	**125**

*Compounds not covered by current generic text.

Scottish Police Authority (SPA) Forensic Services

Data from analysis of drugs seized in Scotland by the SPA forensic laboratory are summarised in Table 16. Mephedrone was by far the most common substance detected. There were no detections of MDPHP but some detections of α-PVP were documented. No synthetic cathinones currently outside the scope of the MDA generics were detected.

Table 16. Synthetic cathinones detected in samples seized in Scotland and analysed by SPA Forensic Services

Synthetic cathinone	2019	2020	2021	2022	2023	Total
Mephedrone		116	104	102	141	463
CMC (not specified)	3	1	14	22	35	75
Eutylone	3	3	26	21	2	55
CEC (not specified)	10	5	3	2	1	21
N-Ethylhexedrone	7	7	3			17
Mexedrone		5	3			8
Dipentylone				4		4
N-Ethylheptedrone		3	1			4
MEC (not specified)	2		2			4
α-PVP				3		3
Ephylone			1		1	2
N-Butylpentylone			1	1		2
Pentylone		1	1			2
α-PiHP				2		2
Methylone	1					1
N-Methylmethedrone				1		1
Ephedrone					1	1
TOTAL	**26**	**141**	**159**	**158**	**181**	**665**

Episodes of toxicity

IONA Study

The Identification of Novel Psychoactive Substances (IONA) study collected clinical data and analysed biological samples (blood and/or urine) from consenting patients attending 39 participating UK emergency departments with suspected toxicity due to substance use between March 2015 and March 2023. Over the 8 years of the study, samples from 1,815 patients were analysed and 89 samples contained one or more synthetic cathinones. Cathinones were the fourth most frequent new psychoactive substance category detected, after synthetic cannabinoid receptor agonists (565 detections), NPS benzodiazepines (504 detections) and new synthetic opioids (151 detections).

The number of patients recruited differs from year to year, so this need to be accounted for by dividing detection numbers by the number of patients to produce a detection rate. Detection rates for synthetic cathinones were lower towards the end of the study, but small numbers limit the conclusions that can be drawn.

Individual substances detected are shown by year in Table 17. Mephedrone was the most common substance detected, but detections of this compound declined in the later years of the study. Ephylone also had more than 10 detections overall, but was not detected after 2019.

There were 3 detections for MDPHP, 1 in 2017 and 2 in 2018. These cases are described in more detail in paragraph 13.17.

Table 17. Percentage of consenting ED patients in IONA study with specific synthetic cathinones in at least one sample, March 2015 to March 2023

	2015*	2016	2017	2018	2019	2020	2021	2022	2023*	Total
Annual patient numbers (n)	56	179	225	170	221	193	262	396	113	**1,815**
Mephedrone	4%	2%	1%	1%	0%	3%	2%	2%	1%	**27**
Ephylone	0%	1%	0%	2%	3%	0%	0%	0%	0%	**11**
4-CMC	0%	1%	0%	0%	0%	0%	1%	0%	1%	**7**
Eutylone	0%	0%	0%	0%	0%	1%	2%	0%	1%	**6**
Methylone	2%	1%	1%	1%	0%	0%	0%	0%	0%	**6**
4-CEC	0%	0%	1%	1%	0%	0%	0%	0%	0%	**4**
Cathinone	0%	2%	0%	1%	0%	0%	0%	0%	0%	**4**
α-PVP	2%	1%	0%	0%	0%	0%	0%	0%	0%	**4**
4-MEC	0%	2%	0%	0%	0%	0%	0%	0%	0%	**3**
MDPHP	0%	0%	0%	1%	0%	0%	0%	0%	0%	**3**
Ephedrone	0%	1%	0%	0%	0%	0%	0%	0%	0%	**3**
Mexedrone	0%	1%	0%	0%	0%	0%	0%	0%	0%	**3**
Butylone	0%	1%	0%	0%	0%	0%	0%	0%	0%	**2**
Pentylone	0%	0%	0%	0%	0%	0%	0%	0%	1%	**2**
Brephedrone	0%	0%	0%	0%	0%	1%	0%	0%	0%	**1**
Cathine	0%	1%	0%	0%	0%	0%	0%	0%	0%	**1**
N-ethylhexedrone	0%	0%	0%	0%	0%	1%	0%	0%	0%	**1**
α-PPP	0%	0%	0%	1%	0%	0%	0%	0%	0%	**1**
TOTAL	**7%**	**12%**	**6%**	**6%**	**4%**	**4%**	**4%**	**2%**	**4%**	**89**

*Part year

ASSIST study

The ASSIST ('A Surveillance Study of Illicit Substance Toxicity') study, conducted by the emergency department (ED) at the Queen Elizabeth University Hospital in Glasgow, has been funded by the Scottish Government since August 2022. Its aim is to monitor drug trends and associated clinical features through the use of prospective surveillance of ED patients attending the ED due to acute illicit drug toxicity. For the sickest patients, the study performs full toxicological analysis through the biorepository-approved surplus sampling. The study collects anonymised clinical data and toxicology testing is performed on surplus serum samples that were taken as part of normal clinical care.

The study identified 2 cases where a synthetic cathinone was detected, one in 2022 (mephedrone, 95 samples analysed) and one in 2023 (Ephylone, 157 samples analysed).

National Poisons Information Service (NPIS)

The UK Health Security Agency commissions the NPIS to provide information and clinical advice to UK health professionals managing patients who may have been exposed to potentially toxic substances, including drugs of misuse. In most cases, information is provided via an internet database called TOXBASE®, but a 24/7 telephone enquiry line is available with consultant support for more complex cases or when TOXBASE® cannot be accessed. The number of accesses to TOXBASE® and NPIS telephone enquiries reflects (but does not measure directly) the frequency of contacts between health professionals and patients presenting following suspected exposures to different substances. Note that analytical confirmation of suspected exposures is rarely available.

Five-year NPIS telephone enquiry and TOXBASE® access data are shown in Tables 18 and 19 below. Telephone enquiries involving specific cathinones have been very uncommon over this period, although it is important to consider that healthcare professionals and the patients they are treating are often unaware of the precise ingredients of drug products they have used. Over the 5 years, there were only 33 telephone enquiries apparently involving a synthetic cathinone, including 15 where 'monkey dust' was listed as an exposure (Table 18).

Table 18. Annual numbers of telephone enquiries made to the NPIS in relation to synthetic cathinones, by financial year

Synthetic cathinone	2019-20	2020-21	2021-22	2022-23	2023-24	Total
Mephedrone	4	1		4	3	**12**
'Monkey dust'	3	2	2	4	4	**15**
Catha edulis	1				1	**2**
α-PVP	1		1			**2**
4-CMC		1				**1**
Methcathinone		1				**1**
TOTAL	**9**	**5**	**3**	**8**	**8**	**33**

Numbers of enquiries to the TOXBASE® website are higher, but some of these may not be directly patient-related, for example made for interest or educational reasons. There have been no consistent changes in annual numbers of accesses to 'monkey dust' information over the last 4 years. Mephedrone continues to be the most common specific synthetic cathinone that healthcare professionals seek information about (Table 19). Note that no data are available for MDPHP as there appears to be no TOXBASE® entry for this compound.

Table 19. Annual numbers of accesses by registered healthcare professionals to entries about synthetic cathinones on the TOXBASE® website, by financial year

Synthetic cathinone	2019-20	2020-21	2021-22	2022-23	2023-24	Total
Mephedrone	425	500	259	274	355	**1,813**
'Monkey Dust'	90	226	181	203	291	**991**
α-PVP	42	27	36	26	33	**164**
Methylone	86	78	50	46	64	**324**
2,4-DMEC	27	123	53	4	9	**216**
Methedrone	33	44	27	27	24	**155**
N-methyl-bk-MMDA-2	32	14	9	12	8	**75**
MDPV	13	11	14	13	11	**62**
Methcathinone	10	8	13	9	13	**53**
Eutylone	0	6	13	5	7	**31**
MDPEP	0	8	4	4	10	**26**
Ephylone	6	7	5	3	3	**24**
N-ethylhexedrone	3	5	7	2	9	**26**
2-MMC	7	4	4	1	8	**24**
Butylone	6	5	5	5	3	**24**
3F-α-PVP	0	5	8	2	7	**22**
4-CMC	0	3	17	1	1	**22**
TOTAL	**780**	**1074**	**705**	**637**	**856**	**4,030**

Note: Data restricted to cathinones with more than 20 accesses over the 5-year period.

Drug-related deaths

Information on drug-related deaths is available from several sources. These include death registrations, which are collected separately in the various devolved administrations, as well as forensic analysis of samples taken at PM. There is some overlap between these sources but there is value in reporting both as the latter provide more information about specific compounds identified.

Office for National Statistics (ONS)

ONS publishes the annual numbers of drug-related poisonings in England and Wales where new psychoactive substances were mentioned on death certificates. The data includes cathinones as a group and mephedrone separately. It is possible to calculate deaths involving all cathinones other than mephedrone, but data on other individual cathinones is not available. Deaths involving mephedrone increased between 2010 and 2015, but have subsequently declined. Deaths involving other cathinones have, collectively, been more common than those for mephedrone since 2015 (Table 20) but remain relatively uncommon. To put these data in perspective, the 9 cathinone-related deaths in 2022 are a small component of the 4,907 drug-

related deaths registered in that year, including 934 for heroin and morphine, 857 for cocaine, 241 for all new psychoactive substances combined, 181 for amphetamine and 51 for MDMA.

Table 20. Annual numbers of drug-related poisonings in England and Wales where a cathinone was mentioned on the death certificate; data provided for cathinones as a whole and for mephedrone for deaths registered between 2009 and 2022

	Substance		
Year	**Cathinones**	**Mephedrone**	**Other (all minus mephedrone)**
2009	0	0	0
2010	6	6	0
2011	6	5	1
2012	18	12	6
2013	26	18	8
2014	27	22	5
2015	49	44	5
2016	31	15	16
2017	7	1	6
2018	16	2	14
2019	14	1	13
2020	6	3	3
2021	16	4	12
2022	9	1	8

ONS has also provided additional data on 20 specific synthetic cathinones. These are for the numbers of drug-related poisonings in England where any of these were mentioned on the death certificate for the 5 years 2018 to 2022 (Table 21). Over this period, the synthetic cathinones most commonly involved in these deaths were MDPHP, α-PHP and mephedrone.

Note that no deaths were recorded during this period where any of the following were mentioned on the death certificate: FMC (not specified), MEC (not specified), cathine, eutylone, pentylone or α-PVP.

Table 21. Annual numbers of cases where the listed synthetic cathinones were mentioned on death certificates in cases of drug-related poisoning, England and Wales, 2018 to 2022

	2018	**2019**	**2020**	**2021**	**2022**	**Total**
MDPHP	1	10	0	2	5	18
α-PHP	0	0	2	8	5	15
Mephedrone	2	1	3	4	1	11
Cathinone (unspecified)	5	0	0	0	0	5
Methylenedioxypyrovalerone (MDPV)	3	0	1	1	0	5
Butylone	2	0	0	1	0	3

	2018	2019	2020	2021	2022	Total
Dibutylone	1	1	0	1	0	3
4-Methylpentedrone	2	0	0	0	0	2
4-MEC	1	0	0	0	0	1
Methylone	1	0	0	0	0	1
Methedrone	0	0	0	1	0	1
4-CMC	0	0	0	1	0	1
Mexedrone	0	0	1	0	0	1
TOTAL	**18**	**12**	**7**	**19**	**11**	**67**

National Records of Scotland (NRS)

Data from the NRS provided to the EU-MADNESS study includes 5 cases where mephedrone has been implicated as the cause of death, one in 2019, one in 2020, 2 in 2021 and one in 2022. In 2 cases, no other psychoactive substances were detected, In the other 3 cases other substances were detected specifically alcohol and mirtazepine (one case), quetiapine (one case) and lamotrigine and cocaine (one case). No other synthetic cathinones were implicated as a cause of death.

Four further cases were reported where a synthetic cathinone was detected in PM toxicology. In 3 cases, this was mephedrone (2 cases in 2020 and one in 2022) and in one case, eutylone (2023). Other psychoactive substances were also detected in all 4 cases.

Public Health Scotland (PHS)

PHS reported 7 deaths in Scotland in which a synthetic cathinone has been detected in PM samples since 2019, mephedrone in all cases (one in 2019, 3 in 2022 and 3 in 2023). It is not clear to what extent these cases overlap with those reported by the NRS or the SPA.

Scottish Police Authority (SPA)

The SPA has provided details of 19 deaths where either mephedrone (18 cases, 16 male) or naphyrone (1 male case) were detected in samples taken during a PM since 2010. They were unable to report data for other synthetic cathinones. Years of death were provided for 11 patients and are shown in Table 22. Age was available for 12 of the patients and ranged from 18 to 52 years (Median 32 years). Mephedrone was the only psychoactive substance detected in one patient, and mephedrone with alcohol alone in a second patient. Multiple psychoactive substances were detected in the other 17 patients in addition to mephedrone or naphyrone. Again, it is not clear to what extent these cases overlap with those reported by the NRS or PHS.

Table 22. Deaths reported by SPA in which either mephedrone or naphyrone were detected at PM, 2010 to 2022

Year	Synthetic cathinone	
	Mephedrone	Naphyrone
2010	4	1
2011	0	
2012	1	
2013	1	
2014	1	
2015		
2016		
2017		
2018		
2019	1	
2020		
2021		
2022	1	
2023		
2024	1	
Year not recorded	8	

Northern Ireland Statistics and Research Agency (NISRA)

NISRA has provided details of deaths registered with the General Registration Office in Northern Ireland for the period 2019 to 2023. There were 9 deaths in which a synthetic cathinone was involved, 3 involving mephedrone, 3 involving MMC (not specified) and one 4-CEC (Table 23).

Table 23. Registered deaths involving a synthetic cathinone, Northern Ireland, 2019 to 2023

Synthetic cathinone	2019	2020	2021	2022	2023
MMC (not specified)				1	3
4-CEC		1			
Mephedrone		1			2
Eutylone		1			

NPSUM

The National Programme on Substance Use Mortality (NPSUM, formerly known as NPSAD) receives drug-related death reports made voluntarily by coroners across England, Wales and Northern Ireland, but not Scotland. Approximately 90% of jurisdictions now provide reports to NPSUM, with exceptions (as of 1 Feb 2024) including the Black Country, Coventry, Worcestershire, Warwickshire,

Gloucestershire, North London, Inner North London, Inner West London, Inner South London and South London.

NPSUM provided data on reports received by 1 February 2024 involving 5 synthetic cathinones since 2010 and for a further 29 synthetic cathinones for the period 2019 to 2023.

Annual numbers of deaths involving any synthetic cathinone have fallen since 2010, with this fall contributed to by reductions in cases involving mephedrone and MDPV. Peak annual numbers of deaths were documented for α-PVP in 2016, MDPHP in 2018 and α-PHP in 2021 (Table 24). Note that because the average delay between death and conclusion of a coronial inquest in the UK is currently 10 to 13 months, further deaths that occurred during this period (and especially during 2023) are likely to be reported in due course.

A total of 75 deaths (62 males, 83%) involving one of more of the 34 synthetic cathinones were reported for the period 2019-2023, involving 93 different cathinone detections (2 different cathinones involved in 12 deaths and 3 different cathinones in 3 deaths). The mean age was 40 years, with 93% aged over 25 years. According to postcode, 33% were in the lowest 2 deciles of social deprivation and a further 9% were of no fixed abode. More than half were unemployed and 84% were known drug users. More than half of the deaths (52%) were reported from Staffordshire, despite some of south Staffordshire falling within the Black Country authority, from which data are not available.

Demographic information was provided by individual synthetic cathinone for mephedrone and 4 pyrovalerone synthetic cathinones of interest for the 62 deaths involving these compounds during 2019 to 2023 (Table 25), although data for MDPV is not presented here as there was only one death involving this compound during that period. Compared to those involving mephedrone, deaths involving the other 3 pyrrolidino-cathinones involved a higher proportion of females, older people, lower deprivation indices by postcode or higher proportions of those affected who were of no fixed abode, higher rates of unemployment and higher proportions of known drug users. (Table 25). Almost every case had other drugs detected, commonly amphetamines or cocaine, and many of these deaths involved more than one cathinone. These included one of the 21 of the deaths involving mephedrone (with mexedrone, MDPV and α-PVP), 8 of the 15 involving MDPHP (with α-PHP in 5 cases and α-PVP in 3 cases), 5 of the 28 involving α-PHP (all with MDPHP) and 4 of the 7 involving α-PVP (with MDPHP in 3 cases and mephedrone, mexedrone and MDPV in 1 case).

Table 24. Synthetic cathinones detected in deaths reported to NPSUM, 2010 to 2023

Synthetic Cathinone	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
α-PHP	0	0	0	0	0	0	0	1	1	1	7	16	3	1
Mephedrone	55	27	26	31	32	39	7	4	5	4	3	8	2	4
MDPHP	0	0	0	0	0	0	0	11	15	1	3	4	7	0
α-PVP	0	0	0	0	2	4	8	0	1	1	0	3	3	0
MDPV	9	5	1	1	1	1	0	0	0	0	0	1	0	0
Dibutylone	0	0	0	0	0	0	0	1	0	2	5	0	0	0
Eutylone	0	0	0	0	0	0	0	0	0	0	3	0	0	0
Methylone	0	0	4	9	3	1	0	1	0	0	2	0	0	0
Ephylone	0	0	0	0	0	0	1	4	2	1	0	0	0	1
Methedrone	2	3	0	1	0	0	0	0	0	0	0	1	1	0
Pyrovalerone	1	0	0	0	0	0	0	0	0	0	0	0	0	0
Ethylone	0	0	0	1	2	3	0	0	0	0	1	0	0	0
Butylone	0	0	0	1	0	3	0	3	0	1	0	0	0	0
Pentylone	0	1	0	0	0	0	0	0	0	0	1	0	0	0
Benzedrone	0	0	0	0	0	0	0	0	0	0	0	0	1	0
3-MMC	0	0	0	0	0	0	0	0	1	0	1	0	0	0
TOTAL	**67**	**36**	**31**	**44**	**40**	**51**	**16**	**25**	**25**	**11**	**26**	**33**	**17**	**6**

Notes:

Data are available for 34 compounds for 2019 to 2023, as listed in and below the table. Note that more than one compound may be detected in the same fatal case.

No deaths were reported between 2019 and 2023 involving N-desalkyl-4-methylmethcathinone (4-methylcathinone or normephedrone), naphyrone, flephedrone, MDPBP, 3-fluoroephedrine, 4-fluoroephedrine, 3-FMC, FMC (not specified), pentedrone, MEC (not specified), 4-CMC, Methyl N-ethylpentedrone , 4-CEC, N-ethylhexedrone, fluorocathinone, 4C-PVP, benzedrone, 3-CMC, dipentylone and/or α-PiHP.

Table 25. Demographic information for cathinone-related deaths involving mephedrone, MDPHP, α-PHP and α PVP, 2019 to 2023

	Mephedrone	MDPHP	α-PHP	α-PVP
n=	21	15	28	7
Sex	%	%	%	%
Male	90.5	73.3	82.1	85.7
Female	9.5	26.7	17.9	14.3
Age range	%	%	%	%
15-24	14.3	-	-	-
25-34	19.0	26.7	10.7	-
35-44	52.4	33.3	32.1	42.9
45-54	9.5	33.3	50.0	14.3
55-64	4.8	6.7	7.1	42.9
Decile of deprivation	%	%	%	%
1	19.0	46.7	35.7	28.6
2	9.5	20.0	21.4	14.3
3	4.8	-	14.3	14.3
4	9.5	-	10.7	-
5	23.8	-	7.1	-
6	9.5	-	-	-
7	4.8	-	3.6	-
8	9.5	6.7	-	14.3
9	4.8	-	-	28.6
10	0.0	-	-	-
No fixed abode	4.8	26.7	7.1	-
Drug user	%	%	%	%
Yes	52.4	100.0	100.0	100.0
No	4.8	-	-	-
Not known	42.9	-	-	-
Employment status				
Unemployed	19.0	80.0	89.3	57.1
Employed	42.9	6.7	3.6	14.3
Homemaker	-	6.7	-	28.6
Student/pupil	9.5	-	-	-
Retired	-	-	3.6	-
Not known	28.6	6.7	3.6	-

Note:

*Data are not presented for MDPV as there was only one death involving these compounds during this period.

There were also important geographic differences, with all but 1 of the 15 MDPHP deaths (93%), all of the 28 α PHP deaths (100%) and 4 of the 7 α-PVP deaths (57%) reported from Staffordshire. Manchester provided the largest numbers of mephedrone-related deaths. Of note, there were no mephedrone-related deaths reported from Staffordshire (Table 26). The compounds α-PHP, α-PVP, MDPHP and MDPV contributed 38 of the 262 drug-related deaths (14.5%) documented by NPSUM for Staffordshire. Note that data for

2023 in particular is incomplete as there is a delay of more than one year between death and conclusion of the relevant inquest in Staffordshire (Table 27).

Table 26. Location of death for cathinone-related deaths involving mephedrone, MDPHP, α-PHP and α-α-PVP, 2019 to 2023

	Mephedrone	MDPHP	α-PHP	α-PVP
n=	21	15	28	7
Location of death	%	%	%	%
Cumbria	-	-	-	-
Lancashire	4.8	-	-	-
Manchester	23.8	-	-	-
Yorkshire	14.3	-	-	-
Derbyshire	-	-	-	14.3
Leicestershire	-	-	-	-
Staffordshire	-	93.3	100.0	57.1
Shropshire	-	-	-	14.3
Birmingham	4.8	-	-	-
Norfolk	4.8	6.7	-	-
West London	9.5	-	-	-
Berkshire	-	-	-	-
Surrey	4.8	-	-	-
Hampshire	4.8	-	-	14.3
Sussex	9.5	-	-	-
Brighton & Hove	4.8	-	-	-
South Wales Central	4.8	-	-	-
Northern Ireland	9.5	-	-	-

**Data are not presented for MDPV as there was only one death involving this compound during this period.*

Table 27. Drug-related deaths in Staffordshire reported to the NPSUM study, 2019 to 2023

Year	Deaths with selected cathinones*	Total deaths	% of total deaths with selected cathinones
2019	3	80	3.8
2020	7	73	9.6
2021	18	63	28.6
2022	9	43	20.9
2023	1	3	33.3
Total	**38**	**262**	**14.5**

Annex D: Possible re-modelling the cathinone generic controls

The current wording of the paragraphs addressing generically controlled cathinones in Part II of Schedule 2 of the Misuse of Drugs Act 1971 (Class B drugs) is as follows:-

(aa) Any compound (not being bupropion, cathinone, diethylpropion, pyrovalerone or a compound for the time being specified in sub-paragraph (a) above) structurally derived from 2-amino-1-phenyl-1-propanone by modification in any of the following ways, that is to say,

- *(i) by substitution in the phenyl ring to any extent with alkyl, alkoxy, alkylenedioxy, haloalkyl or halide substituents, whether or not further substituted in the phenyl ring by one or more other univalent substituents;*
- *(ii) by substitution at the 3-position with an alkyl substituent;*
- *(iii) by substitution at the nitrogen atom with alkyl or dialkyl groups, or by inclusion of the nitrogen atom in a cyclic structure.*

(ab) Any compound structurally derived from 2-amino-propan-1-one by substitution at the 1-position with any monocyclic, or fused-polycyclic ring system (not being a phenyl ring or alkylenedioxyphenyl ring system), whether or not the compound is further modified in any of the following ways, that is to say,

- *(i) by substitution in the ring system to any extent with alkyl, alkoxy, haloalkyl or halide substituents, whether or not further substituted in the ring system by one or more other univalent substituents;*
- *(ii) by substitution at the 3-position with an alkyl substituent;*
- *(iii) by substitution at the 2-amino nitrogen atom with alkyl or dialkyl groups, or by inclusion of the 2-amino nitrogen atom in a cyclic structure.*

The same wording is used in Schedule 2 of the Misuse of Drugs Regulations (Schedule 1 drugs) and in the Misuse of Drugs (Designation) Order 2015.

To bring cathinones that, like α-D2PV, have the third carbon of their sidechain incorporated into a phenyl ring within the scope of these controls, sub-paragraph (ii) of each of the 2 paragraphs within each piece of legislation can be expanded by addition of the words “or by inclusion of the carbon atom at the 3-position in a phenyl ring”. This would bring α-D2PV and closely related materials under control as Class B, Schedule 1 materials, designated as drugs to which para 7(4) of the Misuse of Drugs Act 1971 applies. This revision would, for example, include indapyrophenidone. Although the ACMD has not specifically recommended this compound for control, due to current lack of data regarding levels of use and harm within the UK, its capture by this revision of the generic does not produce any specific disadvantages.

Annex E: List of abbreviations used in this report

ACMD	Advisory Council on the Misuse of Drugs
5-HT	5-Hydroxytryptamine (Serotonin)
CEC	Chloroethcathinone
CMC	Chloromethcathinone
CSEW	Crime Survey for England and Wales
DAT	Dopamine transporter
DEA	Drug Enforcement Administration
DSTL	Defence Science and Technology Laboratory
ED	Emergency department
EDIT	Evidential Drug Identification Testing
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
ENDD	European New Drugs Database
EUDA	European Union Drugs Agency
EURO-DEN Plus	European Drug Emergencies Network Plus Study
EU-MADNESS	EUropean-wide, Monitoring, Analysis and knowledge Dissemination on Novel/Emerging pSychoactiveS
FSNI	Forensic Science Northern Ireland
FTIR	Fourier Transfer Infrared Spectrometry
GC-MS	Gas Chromatography Mass Spectroscopy
ICSS	Intracranial self-stimulation
IM	Injected intramuscularly
IONA	Identification of Novel Psychoactive Substances
IUPAC	International Union of Pure and Applied Chemistry
IV	Intravenously
MANDRAKE	Manchester Drug Analysis and Knowledge Exchange
MDA	Misuse of Drugs Act 1971
mCPP	meta-chlorophenylpiperazine
MDPHP	3',4'-Methylenedioxy-α-Pyrrolidinohexiophenone
MDR	Misuse of Drugs Regulations 2001
MEC	Methylethcathinone
MHRA	Medicines and Healthcare Products Regulatory Agency
MMC	Methylmethcathinone
MoRILE	Management of Risk in Law Enforcement
MRC	Medical Research Council

NCA	National Crime Agency
NET	Norepinephrine transporter
NIHR	National Institute for Health and Care Research
NISRA	Northern Ireland Statistics and Research Agency
NPIS	National Poisons Information Service
NPS	Novel psychoactive substances
NPSUM	The National Programme on Substance Use Mortality
NRS	National Records of Scotland
OHID	Office For Health Improvement and Disparities
ONS	Office for National Statistics
PHS	Drugs Team at Public Health Scotland
PM	Post-mortem
PSA	Psychoactive Substances Act 2016
SCRAs	Synthetic Cannabinoid Receptor Agonists
SERT	Serotonin transporter
SPA	Scottish Police Authority
UN	United Nations
UNODC	United Nations Office on Drugs and Crime
VMAT2	Vesicular monoamine transporter-type 2
WEDINOS	Welsh Emerging Drug and Identification of Novel Substances

Annex F: Chair and members of ACMD Synthetic Cathinones Working Group

Chair of Working Group	
Professor Simon Thomas	Emeritus Professor of Clinical Pharmacology and Therapeutics, Newcastle University
Members of Working Group	
Mr Peter Cain	Drugs Scientific Advisor, Eurofins Forensic Services
Dr Caroline Copeland	Senior Lecturer in Pharmacology and Toxicology, King's College London, and Director of the National Programme on Substance Use Mortality (NPSUM)
Dr John Martin Corkery	Associate Professor in Psychoactive Substances' Epidemiology, Toxicology and Mortality, University of Hertfordshire, and epidemiological lead for EU-MADNESS project
Professor Colin Davidson*	Professor of Neuropharmacology, University of Central Lancashire and pharmacology lead for EU-MADNESS project
Professor Jim Docherty*	Emeritus Professor, Royal College of Surgeons in Ireland and Press Editor, British Journal of Pharmacology
Ms Sophia Fedorowicz*	Research and Evaluations, Expert Citizens CIC
Dr Carl Fletcher*	Principal Scientist at UK Border Force and DSTL
Mr Robert Hessell*	DCI, CID South, Staffordshire Police
Professor Stephen Husbands	Professor of Medicinal Chemistry, University of Bath
Mr Guy Jones*	Technical Lead, Reagent Tests UK and Senior Scientist, The Loop
Mr Colin Mattinson*	DCI, PPU Command, Staffordshire Police
Professor Sarah Page*	Associate Professor in Social Justice and Social Learning, University of Staffordshire
Dr Alberto Oteo Perez*	Senior Executive Drugs Research and Surveillance, OHID and Consultant in Public Policy, EMCDDA
Dr Oliver Sutcliffe*	Director of MANDRAKE and Reader at Manchester Metropolitan University
Mr Ric Treble	Retired Laboratory of the Government Chemist (LGC) Expert
Dr David Wood	Consultant Physician and Clinical Toxicologist, Guy's and St Thomas' NHS Foundation Trust and Reader in Clinical Toxicology at King's College London
ACMD Secretariat	
Miss Lydia Chaloner	ACMD Secretariat

*Co-opted members of the ACMD Working Group

Annex G: ACMD novel psychoactive substances (NPS) committee membership, at time of publication

Mr Paul Bunt**	Director of Casterton Event Solutions Ltd, Former Drug Strategy Manager for Avon and Somerset Constabulary
Mr Peter Cain**	Drugs Scientific Advisor, Eurofins Forensic Services
Dr Caroline Copeland	Senior Lecturer in Pharmacology and Toxicology, King's College London, and Director of the National Programme on Substance Use Mortality (NPSUM)
Dr John Martin Corkery**	Associate Professor in Psychoactive Substances' Epidemiology, Toxicology and Mortality, University of Hertfordshire, and epidemiological lead for EU-MADNESS project
Professor Colin Davidson	Professor of Neuropharmacology, University of Central Lancashire
Dr Hilary Hamnett	Associate Professor in Forensic Science, University of Lincoln, ACMD member
Professor Graeme Henderson	Professor of Pharmacology, University of Bristol, ACMD member
Professor Stephen Husbands	Professor of Medicinal Chemistry, University of Bath
Professor Roger Knaggs	Professor of Pain Management and Clinical Pharmacy Practice, University of Nottingham, ACMD member
Professor Fiona Measham**	Professor and Chair in Criminology, University of Liverpool and Co-Founder of the Loop
Dr Richard Stevenson	Emergency Medicine Consultant, Glasgow Royal Infirmary, ACMD member
Professor Simon Thomas	ACMD NPS Committee Chair; Emeritus Professor of Clinical Pharmacology and Therapeutics, Newcastle University
Mr Ric Treble**	Retired Laboratory of the Government Chemist (LGC) Expert
Professor Derek Tracy	Chief Medical Officer, South London and Maudsley NHS Foundation Trust, ACMD member
Dr David Wood	Consultant Physician and Clinical Toxicologist, Guy's and St Thomas' NHS Foundation Trust and Reader in Clinical Toxicology at King's College London, ACMD member

**Co-opted members of the NPS Committee

Annex H: ACMD membership, at time of publication

Professor Judith Aldridge	Professor of Criminology at University of Manchester
Professor Owen Bowden-Jones	Chair of Advisory Council on the Misuse of Drugs; Consultant Psychiatrist, Central North-West London NHS Foundation Trust
Professor Anne Campbell	Professor of Substance Use and Mental Health, and Co-Director of the Drug and Alcohol Research Network at Queens University, Belfast
Dr Caroline Copeland	Senior Lecturer in Pharmacology & Toxicology, King's College London. Director, National Programme on Substance Use Mortality
Professor Colin Davidson	Professor of Neuropharmacology, University of Central Lancashire
Mr Mohammed Fessal	Chief Pharmacist, Change Grow Live
Miss Bethan Gibbs	Senior Mental Health Clinician, Specialist Social Worker, NELFT
Professor Amira Guirguis	Professor of Pharmacy, MPharm Programme Director at Swansea University Medical School
Dr Hilary Hamnett	Associate Professor in Forensic Science, University of Lincoln
Mr Jason Harwin	Director and Co-founder of E-T-E Solutions Limited
Professor Graeme Henderson	Lead Pharmacist at the Alcohol and Drug Recovery Services, NHS Greater Glasgow and Clyde
Professor Katy Holloway	Professor of Criminology, University of South Wales
Dr Carole Hunter	Chair SDF Board. Doping Control Officer UK Antidoping
Professor Stephen Husbands	Professor of Medicinal Chemistry, University of Bath
Professor Roger Knaggs	Professor in Pain Management and Clinical Pharmacy Practice, University of Nottingham
Mrs Sapna Lewis	Senior Lawyer, Welsh Government Legal Services Department
Mrs Fiona Spargo-Mabbs	Director and Founder, Daniel Sargo- Mabbs Foundation. Chair, Drug Education Forum.
Dr Richard Stevenson	Emergency Medicine Consultant, Glasgow Royal Infirmary
Professor Paul Stokes	Professor of Mood Disorders and Psychopharmacology, King's College London
Professor Harry Sumnall	Professor in Substance Use, Liverpool John Moores University (LJMU)
Professor Simon Thomas	Emeritus Professor of Clinical Pharmacology and Therapeutics, Newcastle University
Professor Derek Tracy	Medical Director of West London NHS Trust

Ms Rosalie Weetman	Public Health Lead (Alcohol, Drugs and Tobacco), Derbyshire County Council and Programme Manager, Drug and Alcohol Improvement Support Team
Dr David Wood	Consultant Physician and Clinical Toxicologist, Guy's and St Thomas' NHS Foundation Trust and Reader in Clinical Toxicology at King's College London

Annex I: Range and quality of evidence

This report drew on evidence from peer-reviewed literature (UK and international publications) and government reports and considered international approaches. Evidence gathered was considered in line with the ACMD's standard operating procedure for quality of evidence (ACMD, 2020).

The ACMD welcomed written submissions on synthetic cathinone use via a public Call for Evidence. Various individuals and organisations throughout the UK participated. The data gathered from received submissions is presented within the report alongside information from peer-reviewed research.

To evidence the identification and prevalence in the UK of the substances considered in this report, the ACMD's Secretariat wrote to stakeholders requesting available data on the synthetic cathinones they had encountered. Responses were received from the following:

Drug seizure and submitted sample analysis data:

- Border Force
- Drugs Team at Public Health Scotland (PHS) (RADAR)
- Emerging Drugs and Technologies Programme (EDAT)
- Manchester Drug Analysis and Knowledge Exchange (MANDRAKE)
- Office for Health Improvement and Disparities (OHID)
- Scottish Police Authority (SPA), Drug Detections
- Scottish Prison Service
- TICTAC
- Welsh Emerging Drugs and Identification of Novel Substances (WEDINOS)

Drug poisoning data:

- A Surveillance Study of Illicit Substance Toxicity (ASSIST)
- Identification of Novel Psychoactive Substances (IONA) study
- National Poisons Information Service (NPIS)

Mortality and post-mortem forensic analysis data:

- Eurofins Forensic Services
- European-Wide, Monitoring, Analysis and Knowledge Dissemination on Novel/Emerging Psychoactive (EU-MADNESS)
- Forensic Science Northern Ireland (FSNI)
- National Programme on Substance Use Mortality (NPSUM)
- NHS Grampian
- Northern Ireland Statistics and Research Agency (NISRA)

- Office for National Statistics (ONS)
- Scottish Police Authority (SPA), Criminal Toxicology
- Scottish Police Authority (SPA), Post-Mortem Toxicology

The ACMD also sought information on whether there were medicinal uses of synthetic cathinones from the Medicines and Healthcare products Regulatory Agency (MHRA).

It is important to note that forensic analysis is inconsistent across the UK and as a result, some ‘novel’ compounds present in samples may not be identified. Consequently, the information being fed into reporting agencies that were approached may not be representative and it remains possible that some synthetic cathinones that are already in circulation in the UK have not yet been identified.

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