ACMD

Advisory Council on the Misuse of Drugs

ACMD Report – A review of the evidence on the use and harms of Xylazine, Medetomidine and Detomidine

Contents

1. Introduction

1.1. Xylazine is a non-opioid tranquilizer approved for use as a sedative, muscle relaxant and analgesic in veterinary medicine, however is increasingly being used illicitly by humans internationally and in the UK.

1.2. Xylazine is a psychoactive adulterant which can be added to heroin or illicitly manufactured fentanyl (IMF), to produce a mixture which is known as FAAX (Fentanyl Adulterated or Associated with Xylazine), 'tranq' or 'tranq dope' in the USA. Xylazine, especially in combination with other sedatives, can dangerously lower an individual's level of consciousness. In addition, it can lower an individual's heart rate and, when injected, is reported to be associated with the development of skin ulcers. In November 2022, the United States Food and Drug Administration (FDA) issued an alert to healthcare professionals concerning the increased prevalence in illicit drug overdose deaths involving xylazine. [FDA 2022]

1.3. Xylazine was first detected in illicit drug markets in Puerto Rico around 2001 and subsequently in opioid-related deaths in mainland United States in 2006. Since then the detection of xylazine has been reported to mirror the IMF supply in the United States, starting in the North East and then spreading Southwards and Westward. Xylazine has now been detected in IMF in 48 States and is reported to have been identified in 23% of IMF powder and 7% of fentanyl tablets seized in 2022. [DEA Alert 2022] However, these rates vary widely by US state.

1.4. Data from the National Forensic Laboratory Information System (NFLIS) in the USA has shown an increase in the number of States that have reported xylazine-related deaths. In 2019, 16 states had zero NFLIS xylazine reports which decreased to only 2 States in 2022 (South Dakota and Wyoming). The highest rates of xylazine NFLIS reports per 100 000 residents in 2022 were concentrated in the North Eastern States (New Jersey (30.52), Rhode Island (22.82), Maryland (18.91), Virginia (15.47) and New Hampshire (13.10). [Cano 2024]

1.5. In Canada, xylazine identifications in samples submitted by law enforcement agencies increased from 5 in 2018 to 1350 in 2022, with most positive samples detected in Ontario and British Columbia. Almost all samples contained multiple other substances, most commonly cutting agents (e.g. caffeine or dimethylsulphone), opioids (especially fentanyls but also heroin) and benzodiazepines (e.g. flualprazolam, etizolam, bromazolam). [Health Canada 2023]

1.6. The US Drug Enforcement Administration (DEA) previously suggested xylazine was entering the drug market supply via misdirection of legitimate veterinary sources of xylazine; however, the detection of xylazine in fentanyl tablets produced outside the USA suggests that there may be a shift away from adulteration of IMF in the USA from misdirected veterinary supplies.

1.7. Xylazine may be added to illicit fentanyl supplies in North America due to low purity of fentanyl entering the drug market from Mexico and other areas. It is postulated the addition of the xylazine may enhance the sedative effects seen with fentanyl and potentially interfere with fentanyl metabolism, thereby directly prolonging the desired effects of the fentanyl.

1.8. To date xylazine has been much less frequently detected in Europe than in North America, however mixtures containing xylazine with the synthetic opioids protonitazene or metonitazene have been seized in Estonia. In a survey in Riga, Latvia, xylazine was co-detected in 13% of used syringes, with the synthetic opioids isotonitazene, metonitazene or carfentanil. [EMCDDA Annual Report 2023]

1.9. Currently, injecting drug users in Europe use heroin derived from Afghanistan, which has been of high quality and therefore there has been little use of other illicitly synthesised opioids such as fentanyl, or for the adulteration of illicit opioids with drugs such as xylazine, in contrast to the situation in North America.

1.10. As a result of the prohibition of cultivation of opium poppies and of all types of narcotics in Afghanistan by the Taliban in April 2022, there has been a 95% reduction in the areas cultivating opium poppies between 2022 and 2023. This resulted in a 95% decline in both the opium harvested and export heroin produced from 6,200 tons and 350-580 tons respectively in 2022 and to 333 tons and 24-38 tons respectively in 2023. [UNODC Afghanistan opium survey 2023] There is increasing concern that, with the reduction in availability of heroin from Afghanistan, the European and UK illicit opioid markets may shift to illicitly synthesised fentanyl. There is the potential that this would be associated with increased risk of xylazine in the UK illicit opioid market.

1.11. The first death in the UK involving xylazine was reported by the National Programme on Substance Abuse Deaths (NPSAD) in December 2022.

1.12. As a result of horizon scanning, the ACMD self-commissioned a review into the potential harms of xylazine, and this was followed by a formal government commission in June 2023.

1.13. This report reviews the evidence of use and harms of xylazine in the UK and considers whether it should be controlled via the Misuse of Drugs Act 1971. Evidence of illicit use in the UK of the related compounds medetomidine and detomidine was also sought, as this has been reported in other countries. [CSFRE 2023a; CSFRE 2023b; Sisco 2023]

2. Legal Control

2.1. In the UK, xylazine, detomidine and medetomidine are veterinary medicines licensed for use as sedatives, muscle relaxants and analgesics in animals; more information on their use as veterinary medicines is described in Section 6 below. Only dexmedetomidine (one of the stereoisomers of medetomidine) is approved by the Medicines and Health care products Regulatory Agency (MHRA) for human use, as a sedative for use by infusion in critical care areas.

2.2. Xylazine, detomidine and medetomidine are not currently controlled under the Misuse of Drugs Act 1971. They are, however, likely to be subject to the 2016 Psychoactive Substances Act (PSA) because they have psychoactive effects, given that they are licensed for use as sedatives and/or anaesthetics in veterinary medicine. Whilst these are all veterinary medicines, the list of 'exempted substances' in Schedule 1 of the PSA includes only medicinal products approved for human use and the list of 'exempted activities' in Schedule 2 includes only human applications. Therefore, their import, supply, possession with the intent to supply and possession in a custodial institution for human use are likely to be offences under the PSA. To confirm this and initiate any prosecutions for such offences, the compounds would have to be tested against a panel of receptors as part of the two-stage in vitro testing process conducted by the Defence Science and Technology Laboratory (DSTL). Alternatively, a statement confirming psychoactivity from an expert witness, such as a pharmacologist, pharmacist, or registered veterinary surgeon, could be used to support a prosecution.

3. Chemistry

3.1. Xylazine consists of a 2,6-dimethylphenyl ring linked via an amine bridge to a 5,6-dihydro-1,3-thiazine ring (thiazine being a six-membered heterocycle containing 4 carbon atoms, 1 sulphur and 1 nitrogen).

3.2. A number of structurally similar compounds, which also feature a phenyl ring linked via an amine bridge to a five-membered heterocycle, are pharmaceuticals approved for human use, including clonidine (2,6-dichlorophenylimidazole-2-amine) which is also an alpha-2 receptor agonist although less potent than xylazine. Other similar pharmaceuticals include apraclonidine (licensed in the UK for reducing intra-ocular pressure) and romifidine (approved as a veterinary drug).

3.3. A range of other pharmaceutical compounds have some structurally similarity, featuring a phenyl ring linked via a methyl bridge to an imidazole ring. These include dexmedetomidine, a stereoisomer of medetomidine, which is significantly more potent than clonidine but less potent than xylazine; levomedetomidine, the other stereoisomer of medetomidine is inactive. [Kuusela 2001; Siegenthaler 2020] Others include detomidine, which is also an alpha-2 receptor agonist, and xylometazoline, a nasal decongestant. Lofexidine, used in the management of opioid withdrawal, has a similar structure to clonidine, except that the nitrogen link between the two rings is

replaced by a link consisting of an oxygen atom attached to the phenyl ring joined to the 1-position of an ethyl group attached to the imidazole ring.

3.4. The chemical structures for xylazine, medetomidine and detomidine, along with clonidine and lefoxidine are shown in Appendix A.

4. International control

Xylazine control in the USA

4.1. As of December 2023, xylazine had not yet been brought under the control of the Controlled Substances Act in the USA. However, some individual states have used legislation to schedule at the state level, including Florida, Ohio, West Virginia, Pennsylvania and Illinois.

4.2. Following the designation of fentanyl adulterated and/or associated with xylazine as an emerging drug threat in April 2023, a number of further actions have occurred:

4.2.1. The US Food and Drug Administration issued Import Alert 68-20 in June 2023, permitting the seizure of importations of xylazine and finished products containing xylazine from a 'red list' of suppliers or which appear to have been mis-declared;

4.2.2. The White House released the "Fentanyl adulterated or associated with xylazine emerging threat response plan" in July 2023; and

4.2.3. The US Congress is currently considering Federal legislation (S. 993/H.R. 1839, The Combating Illicit Xylazine Act), which would seek to classify xylazine as a Schedule III Controlled Substance.

Xylazine control in other countries

4.3. Outside the USA, xylazine continues to be considered as a veterinary medicine, subject to national veterinary prescription requirements, rather than as a Controlled Drug.

Detomidine and medetomidine control

4.4. Detomidine and medetomidine are considered as veterinary medicines, subject to national veterinary prescription requirements, rather than as Controlled Drugs.

5. Misuse

5.1. Xylazine, medetomidine and detomidine are not specifically named as compounds/drugs in the Crime Surveys in England, Northern Ireland, Scotland or Wales; therefore, there is no information in regards to their prevalence of use in these administrations.

5.2. Qualitative research in the USA with individuals who inject opioids has provided some insight into the experience of those who are exposed to xylazine when injecting opioids. [Reed 2022; Freidman 2022] This research suggests that with the changing opioid market in the USA from heroin to illicit fentanyl, which has a shorter duration of action, xylazine (along with other sedatives) have been added to prolong the desired effects of the illicit fentanyl being injected. However, many individuals do not like the sedative effects reported with xylazine, and so may try to re-sell on any opioids they believe contain xylazine.

5.3. There is very limited information on user discussion fora relating to the intentional recreational use of xylazine, detomidine and/or medetomidine. The information available describes use by a variety of routes; it appears that the onset of desired effects tends to occur more rapidly when used by injection, followed by rectal insertion and then sublingual administration or oral ingestion. The effects are often described as being unpleasant and sedative in nature and their duration is between 3 and 5 hours. There are insufficient reports reporting doses used to comment on any relationship between dose and effects and/or duration of effects.

5.4. In an anonymous Reddit survey posted seventeen times (between March to August 2022) in the seven subreddits identified as having the highest number of Reddit posts on xylazine, respondents reported on their pattern of use. The majority of respondents were from the USA (44), but 2 were from the UK, 2 from Canada, 1 from Sweden and 1 from Ecuador (the location was not disclosed for 11 respondents). Of the 61 respondents, 74% of reported that they do not seek out to buy/acquire drugs that contain xylazine. The route of use of xylazine-containing drugs were inhalational 20%, nasal insufflation 57%, injection 43% or oral ingestion 3%. Xylazine was most frequently used daily (39% of respondents), but 19% reported use 1-6 times/week, 15% reported 1-4 times per month and 27% reported use a few times a year. [Spadaro 2023]

6. Legitimate Uses

6.1. The ACMD Secretariat contacted the Medicines and Healthcare products Regulatory Agency (MHRA) for any information on the legitimate use, clinical trials and/or marketing authorisation applications of xylazine, medetomidine and detomidine.

6.2. The MHRA confirmed that there were no granted, lapsed, cancelled or pending marketing authorisations for xylazine, detomidine or medetomidine. There have been no clinical trial authorisations for xylazine and there has only been one clinical trial authorisation for detomidine/medetomidine (as dexmedetomidine) in 2006 to 2007, with no clinical trial authorisations since then. Dexmedetomidine (one of the two stereoisomers medetomidine) is approved for use in humans in the UK for sedation in intensive care.

6.3. Xylazine, medetomidine and detomidine are prescription only veterinary medicines (POM-V) licensed for sedation and/or use as pre-medication prior to use of alternative injectable or inhalational anaesthetics. The veterinary medicinal products authorised for use in Great Britain and Northern Ireland are:

i) Xylazine: 13 products containing xylazine for use by injection (intravenous, intramuscular or subcutaneous) routes in horses, cattle, dogs and cats;
ii) Detomidine: 18 products for use by injection (intravenous/intramuscular) or oro-mucosal routes in horses and cattle;
iii) Medetomidine: 15 products for use by injection (intravenous, intramuscular or subcutaneous) in dogs and cats.

Of note, veterinary medicines in the UK are authorised for both specific species AND specific conditions. Where there is no authorised veterinary medicine for a specific species and/or condition, veterinarians are permitted to prescribe/use other authorised veterinary or human medicines based on clinical judgement using a risk-based decision tree called the Cascade.

6.4. The authorised veterinary medicines containing xylazine, detomidine or medetomidine are not currently classified as Controlled Drugs. As such, they are subject only to standard storage, record keeping and destruction requirements in accordance with The Veterinary Medicines Regulations (2013).

7. Pharmacology

7.1. There are three subtypes of alpha-2 adrenoceptors – designated α_{2A}, α_{2B} and α_{2C}. [Listik 2023] Sedation and hypotension appear to result from activation of α_{2A} receptors in the brain, whereas peripheral vasoconstriction likely results from activation of α_{2B} receptors located on the smooth muscle of small diameter blood vessels. Xylazine, detomidine and medetomidine are non-selective α-2 adrenoceptor agonists that activate both central and peripheral α-2 adrenoceptors.

7.2. Xylazine is chemically related to phenothiazine antipsychotics and tricyclic antidepressants. Detomidine is an imidazole derivative. Medetomidine is an equal mixture of two optical isomers: dexmedetomidine and levomedetomidine. [Lamont 2009] All of these compounds are analogues of clonidine.

7.3. Xylazine, detomidine and medetomidine are rapidly absorbed following use by a variety of routes, including oral ingestion, nasal insufflation, rectal insertion and ocular exposure. Injection (intravenous, subcutaneous or intramuscular) of these compounds avoids first-pass metabolism, leading to higher initial peak concentrations. [Capraro 2001; Velez 2006; Ball 2022; Gao 2015; Potoukian 2023]. These compounds have large volumes of distribution related to their high lipophilicity (lipid solubility), as discussed in section 7.5.

7.4. All these compounds have a short half-life of minutes, with overall elimination from the body within a few hours of exposure. The half-life of xylazine is reported as 23-50 minutes [Ruiz-Colon et al, 2014]. The metabolism of xylazine in humans is not well understood, but the main xylazine biotransformation pathway is most likely thiazine ring breakdown leading to formation of 2,6-dimethylaniline (DMA) also known as 2,6-xylidine. The main metabolite of medetomidine is N-methyldexmetomidine. [Malayala 2022; Baselt 2017; Kaur 2011, Gao 2015]

7.5. As these compounds are highly lipophilic (high lipid solubility), they can easily cross the blood-brain barrier. Actions of these compounds at central α-2 receptors lead to sedation, muscle relaxation, reduced pain response and depressed respiratory drive. [Fyffe 1994]

7.6. The overlap between blood concentrations associated with non-fatal and fatal intoxications of xylazine; similar to other drugs and NPS this indicates that there is no defined safe, toxic, or lethal concentration. [Potoukian 2023]

7.7. Several α-2 adrenoceptor antagonists are available that could potentially reverse toxicity associated with α-2 adrenoceptor agonists. Yohimbine, an indole alkaloid derived from the bark of the African tree *Pausinystalia johimb*, and atipamezole, are α-2 adrenoceptor antagonists. Of the two, atipamezole has the highest preference for α-2 over α-1 receptors. Although atipamezole is licensed for the reversal of sedation produced by dexmedetomidine and its racemic mixture medetomidine in dogs and cats, yohimbine is not licensed for the reversal of xylazine sedation in veterinary practice. [Van Metre 1992;

Choon 2023] Tolazoline is an α-2 receptor antagonist licensed for use in the treatment for pulmonary vasospasm in neonates, and the antidepressant mirtazapine is an α-2 receptor antagonist with activity at other types of receptors as well. [Guide to Pharmacology 2023] None of these drugs are currently licensed for the reversal of sedation or other unwanted effects in humans produced by xylazine, medetomidine or detomidine.

8. Health harms

Acute toxicity: Xylazine

8.1. Adverse effects reported with human exposure to xylazine include central nervous system depression, hypotension, bradycardia or tachycardia (slow or fast heart rate), respiratory depression, miosis, hyperglycaemia, and hypothermia. [Ruiz-Colon 2014]

8.2. A systematic review identifying published English language cases of xylazine related toxicity identified from *Web of Science, PubMed, Embase, Google Scholar* and grey literature sources were published in 2023. Of the initial 1,238 articles identified, 34 were assessed to meet the systematic review inclusion criteria. [Ayub 2023] However, on review of this report, one of the included articles was a conference poster presentation where xylazine was mentioned in the title of the presentation but there was no mention in the text of the poster that xylazine had been used.

8.3. Of the remaining 33 publications, 1 was a drug-driving related report, 2 related to xylazine withdrawal, 7 related to deaths where xylazine was detected and/or implicated in the cause of death and 23 related to acute xylazine toxicity. The 23 publications relating to acute xylazine toxicity described a total of 33 individual cases (23 male, 8 female, 2 unknown sex; age range 19 days to 76 years old), of which 9 were accidental exposures, 7 were self-harm/suicide attempts, 7 were recreational/misuse related, 4 were malicious and in 6 the intent was not clear from the publication. The route of exposure was known in 27 patients: injection (IV/IM/SC) in 15, oral ingestion in 6, inhalation in 4, ocular in 1 and combined oral ingestion/injection in 1. The majority of individuals (28, 85%) were drowsy following exposure and 12 of those had associated respiratory depression. Nine patients had a trial of naloxone with no significant clinical effect in 7 patients and a response likely related to concurrent opioid toxicity in 2 patients. Nine individuals with coma and respiratory depression and 5 with coma without respiratory depression required intubation. Hypotension occurred in 9 and bradycardia in 17.

8.4. Four cases of the administration of xylazine to individuals for malicious criminal intent have been reported: i) a 4-year-old child presented with drowsiness in Germany following xylazine administered in an attempted drug-facilitated sexual assault by his god-father and ii) three individuals in their 70s were found drowsy in a hospital in Bangkok, Thailand after consumption of drinks offered to them by strangers. [Andresen-Streichert 2017, Krongvorakul 2018]

8.5. There were 76 xylazine exposures reported to the Texas Poison Center Network (TPCN) between 2000 and 2014. Twenty-eight (36.8%) involved other substances [ketamine (9 cases); tiletamine/zolazepam (5); alcohol (3); detomidine (3); butorphanol (2), cocaine (2), and pentobarbital/phenytoin (2). Forty-nine (64.5%) were unintentional (17 occupational-related and 10 were drug misuse); 24 were intentional (12 suspected attempted suicide; 10 abuse of the drug). Forty-one (53.9%) were male. Symptoms in the 48 patients without reported exposure to other substances were: i) drowsiness/lethargy in

43.8%; ii) bradycardia in 27.1%; iii) hypotension in 10.4%; iv) hypertension in 8.3%; v) slurred speech in 6.3%; vi) Coma in 2.1%; vii) ocular irritation/pain in 8.3%; and viii) respiratory depression in 2.1%. [Forrester 2016]

8.6. In the anonymous Reddit survey conducted between March and August 2022, 48 respondents reported unwanted effects from xylazine; 81% reported increased overdoses/passing out and 17% increased emergency room (ED) visits. [Spadaro 2023]

8.7. Nine Emergency Departments (EDs) in California, Oregon, Michigan, Missouri, Pennsylvania, New Jersey and New York enrolled consecutive patients with suspected opioid overdose between 21 September 2020 and 17 August 2021. [Love 2023] Enrolled patients had serum and/or blood samples taken for routine clinical care and these were subsequently analysed to detect whether opioids and/or other drugs had been used before presentation. Illicit opioid use was defined as the detection of "*heroin, fentanyl or its analogs, nitazene or its analogs or other new synthetic opioids*"; the authors did not state if this was parent drug and/or metabolites. Of the 1,006 patients screened, 395 were enrolled into two groups: i) presence of illicit opioid without xylazine (231 patients); ii) presence of illicit opioid with xylazine (90 patients). There were no differences in the demographics (proportion male and median age), initial observations (systolic blood pressure, heart rate, respiratory rate) and use of naloxone between the two groups. The primary outcomes in this study were cardiac arrest requiring CPR or coma. Cardiac arrest requiring CPR occurred in 4 (4.4%) of the 90 xylazine cases and 33 (14.3%) of the no xylazine cases (p=0.13); modelling demonstrated that the detection of xylazine was associated with a reduced risk of this outcome (adjusted odds ratio 0.30, 95% CI 0.10-0.92). There was no significant difference in the frequency of coma within 4 hours (seen in 26.7% of xylazine cases and 37.7% of no xylazine cases, p=0.063) or coma after 4 hours (seen in 13.3% of xylazine cases and 15.2% of no xylazine cases). Modelling demonstrated that the detection of xylazine was associated with an overall lower risk of developing coma (adjusted odds ratio 0.52, 95% CI 0.29-0.94). The explanation for this finding is uncertain, but one possibility acknowledged by the authors is that those exposed to xylazine had used a lower opioid dose.

8.8. The European Drug Emergencies Network Plus (Euro-DEN Plus) project has had a total of 62,613 cases reported to its registry from October 2013 to December 2021. There have been two reports of acute toxicity related to self-reported use of xylazine, both in November 2021 from Riga, Lativa. A 37-year-old male presented with coma (GCS 4) requiring intubation with a heart of 95 bpm, blood pressure 111/61 mmHg and temperature of 37.8°C following the use of xylazine, benzodiazepines and ketamine. He was treated with naloxone pre-hospital and medically discharged from the ED 41 hours after presentation. A 42-year-old female presented with drowsiness (GCS 10), a heart rate of 85 bpm, blood pressure 90/60 mmHg and temperature of 37.0°C following the use of xylazine and benzodiazepines. She did not require any specific treatment and was medically discharged from the ED 27 hours after presentation. In both cases urine immunoassay testing confirmed only the reported drugs used; nothing else was detected.

Acute toxicity: medetomidine

8.9. There have been no published case reports or series describing acute toxicity related to the use of medetomidine.

Acute toxicity: detomidine

8.10. There are four published reports of detomidine related toxicity (2 male, 2 female; age range 26 to 36 years old), of which 3 were accidental exposures and 1 was self-harm/suicide attempt related. The route of exposure was injection (IV/IM/SC) in 3 and dermal absorption in 1. All four were drowsy following exposure, although none were reported to have associated respiratory depression; 2 had bradycardia, 1 had hypotension and 1 had hypertension. One was treated with naloxone, although they had also accidentally injected an opioid. All four required only a brief period of observation and none required intubation. [Reid 1994, Pohjalanien 2001, Cummins 2005, Hannah 2010]

Chronic toxicity and ulceration: xylazine, medetomidine and detomidine

8.11. Qualitative research, reports in the general media and anecdotal reports from users online and engaged with drug treatment services have suggested a higher incidence of skin ulceration associated with the use of xylazine containing drugs that is normally reported. There have been a small number of peer-review publications which have described this occurrence of xylazine-related ulcers and these are summarised in more detail below.

8.12. A study from Puerto Rico in 2008 analysed drug residues in 370 syringes that had been employed by injecting drug users; xylazine was detected in 139 (37.6%). Xylazine was always co-detected with: i) combined heroin/cocaine (126 syringes); ii) cocaine alone (10); or iii) heroin alone (3); no syringes co-contained fentanyl. The 112 injecting drug users whose syringes contained one or more drug were and divided into those whose syringes contained xylazine (39 users) and those that did not (73 users). There was no difference between the xylazine users and non-xylazine users in terms of gender, age and frequency of injection. Xylazine users were more likely to be living on the streets (64% compared to 37%) and had a significantly higher frequency of skin ulcers (38.5% compared to 6.8%). [Rodriguez 2008]

8.13. On the United States mainland there have been case reports of ulcers occurring in 14 individuals (7 males, 6 females and 1 transgender male to female) from Pennsylvania (7 individuals), Connecticut (3), Ohio (2), Florida (1) and New Jersey (1). All reported injecting fentanyl; 6 reported also injecting cocaine and 3 reported injecting heroin. [Dowton 2023, Malayala 2022, Warp 2023, Ehrman-Dupre 2022, Wei 2023, Rose 2023] Xylazine exposure was based on self-reported use alone (2 patients), self-reported use and positive urine detection (4), positive urine detection without self-reported use (6) or awareness of local detection of xylazine in drug supplies but no confirmation of use or detection in urine (2). One female with injection related upper limb ulceration also had ulcers on her knees, despite not injecting into her legs. [Warp 2023] Management of the ulcers included general wound care, antibiotics and, where required, surgical debridement. Complications of

xylazine-related ulcers were reported in one case series of 6 patients included: bacteraemia (4 patients), osteomyelitis (3), abscesses (2), endocarditis (1), empyema (1) and septic emboli (1). [Wei 2023]

8.14. The cause of the ulcers in individuals injecting xylazine is uncertain. Proposed mechanisms for their development include: i) direct toxicity from xylazine; ii) toxicity of other substances injected; iii) xylazine associated alpha-2 mediated local vasoconstriction; iv) increased frequency of injection into the ulcer site to alleviate pain; v) small vessel xylazine associated vasculopathy/vasculitis; and/or vi) compression due to prolonged frequencies of sedation. Additionally, it is postulated that xylazine may impair ulcer healing through reducing tissue oxygen delivery through α2 mediated local vasoconstriction, as well as leading to α2 mediated reduction in insulin and associated hyperglycaemia.

8.15. There have been no reports of ulcers related to the use of medetomidine or detomidine.

Abuse, dependence and withdrawal: xylazine, medetomidine and detomidine

8.16. There have been no animal studies of dependency and/or withdrawal related to xylazine, medetomidine or detomidine.

8.17. There have been no human reports of dependency and/or withdrawal related to medetomidine or detomidine.

8.18. Drug users in the US have discussed in qualitative research their concerns about the potential risks of xylazine related dependency and the lack of appropriate detoxification protocols for managing xylazine withdrawal. [Reed 2022] There have been two cases of xylazine related withdrawal published and these are discussed in more detail below.

8.19. A 29-year-old female known to use 25 bags of heroin/fentanyl intravenously per day was told by her dealer that the bags also contained xylazine. She noted that she was more sleepy following use of the bags containing xylazine and had different withdrawal symptoms when not using that were not responsive to methadone or buprenorphine. She was admitted for management of leg ulcers thought to have developed over eight months related to xylazine injection. To prevent xylazine withdrawal she was treated with dexmedetomidine and tizanidine, however she developed restlessness, rigors and dysphoria in day 2 of her admission. The administration of tizanidine was discontinued and clonidine was initiated. Her autonomic stability was managed with a loading dose of phenobarbital with a subsequent six-day tapering course. By day 4 of her admission she was no longer experiencing any withdrawal symptoms. [Ehrman-Dupre 2022]

8.20. A 35-year-old male veterinarian was admitted involuntarily to a psychiatric clinic in the Netherlands for detoxification from xylazine. He had a history of regular daily use of methylphenidate whilst studying veterinary medicine, and as his use of this increased he developed insomnia, anxiety, and a loss of

appetite. He started to self-inject xylazine to help sleep about 2 years prior to admission; this escalated to the extent where he was using 500mg xylazine per day. There did not appear to be any clear tolerance to xylazine use and there were no withdrawal effects when not using. On admission he was initially treated with a low dose of clonidine (25 micrograms twice daily) and monitored for withdrawal and physiological symptoms. The dosing of clonidine was titrated based on subjective and objective withdrawal scales; there is no documentation of the actual dose titration used during the admission but during use of clonidine his objective and subjective withdrawal scores gradually improved and clonidine was discontinued one week after initiation. [Mulders 2016]

8.21. An anonymous survey was posted seventeen times (between March to August 2022) in the seven subreddits that had previously been identified as having the highest number of Reddit posts on xylazine. Of 59 xylazine users, 53% reported that they had experienced withdrawal from xylazine. The symptoms of withdrawal were reported by 35 participants and included anxiety (91%), depressed mood (74%), body aches (63%) and cravings (49%). Use of xylazine impacted on participants' perceptions of withdrawal from other drugs, with 57% reporting these were worse, 39% the same and 4% better. [Spadaro 2023]

9. Social harms

9.1. There is no information on the social harms that may be caused by xylazine, medetomidine or detomidine use. For xylazine these harms are likely to reflect the substances it is detected with, i.e. benzodiazepines and cannabis in WEDINOS sample analysis in the UK discussed below and opioids in the USA and Canada.

9.2. The acute toxicity described with exposure to xylazine and detomidine involves drowsiness and coma. There have been four cases where individuals have been intentionally exposed to xylazine by others, including a 4-year-old child exposed with the intent of drug-facilitated sexual assault. [Andresen-Streichert 2017, Krongvorakul 2018] Therefore, there is the potential that individuals may be exposed intentionally to xylazine medetomidine and/or detomidine by other individuals with the intent of causing sedation to facilitate crimes such as robbery, assault and sexual assault.

10. UK Prevalence

10.1. The illicit drug market can be monitored by analysing drugs seized by police or voluntarily submitted by the public for testing or from analysis of blood/urine specimens from people who have used drugs (including those who have died). There is now multifaceted evidence from these sources indicating that xylazine has been detected in the UK illicit drug supply.

10.2. To evidence the identification and prevalence of xylazine, medetomidine and detomidine in the UK, the ACMD's New Psychoactive Substances (NPS) Committee wrote to stakeholders in July 2023 requesting available data on their detections.

WEDINOS

10.3. Funded by Public Health Wales, WEDINOS provides laboratory testing of drug samples volunteered by the community. These are received anonymously by post from either individuals or participating organisations (e.g. substance misuse services, housing and hostels, youth clubs and young people's services, education, night clubs and bars, mental health community teams, Local Authorities, Ambulance Services and the Police). Anonymised test results are publicly available online. There is the potential limitation to the WEDINOS dataset as this is based on individuals sending samples to them for analysis. It is commonly used for tablet analysis but injecting drug users may be less likely to send in samples.

10.4. The publicly available 'sample results' section on the WEDINOS website was searched in November 2023 to identify samples that had been analysed where xylazine, detomidine and medetomidine were identified.

10.5. There were no samples analysed by WEDINOS where detomidine or medetomidine have been detected.

10.6. The samples analysed where xylazine was detected are summarised in the Table 1 below by year of detection, along with the total number of samples in each year, and the purchase intent.

Table 1. Summary of WEDINOS analysed samples where xylazine was detected

Year	Samples Analysed	Xylazine Detected	Purchased Intent of the buyer
April 2019 to March 2020	4,045	1	Crystalline ketamine
April 2020 to March 2021	3,416	0	N/A
April 2021 to March 2022	6,345	0	N/A
April 2022 to March 2023	6,656	8	Diazepam tablets (3*), THC vape liquid (2), Temazepam tablets (1*), Xanex tablets (1), Bromazolam powder (1),
April 2023 to January 2024	Not reported	17	Codeine tablets (8**), Tramadol tablets (2), Heroin (6)***, Street Diamorphine (1)****

*These samples all also contained bromazolam
**One sample also contained dipentylone
***Two samples also contained heroin and metabolites. The others samples contained a range of other recreational drugs and NPS: metonitazene (3 samples), protonitazene (3), bromazolam (3), nitrazolam (3) and isotonitazene (1)
****Also contained metonitazene, isotonitazene, heroin, bromazolam and nitrazolam

10.7. Samples positive for xylazine have been submitted from all of the UK except for Northern Ireland. By financial year: 2019/20: Scotland; 2022/23: England 3, Scotland 1, Wales 4; and 2023/24 (to January 2024): England 10, Scotland 4, Wales 3).

Forensic Early Warning Service (FEWS)

10.8. The Forensic Early Warning System (FEWS) has reported no detections of xylazine, medetomidine or detomidine.

10.9. Additional evidence for the spread of illicit xylazine comes from drug seizures made by law enforcement in London (one in 2022, two in 2023), Northamptonshire (2023), and the East of England (2023; CSC personal communication with the Office for Health Improvement & Disparities and the Metropolitan Police).

Office for Health Improvement and Disparities (OHID)

10.10. OHID was officially launched in October 2021 as a part of the Department of Health and Social Care, with the aim of tackling health inequalities across the country.

10.11. Details of samples seized by the police and analysed by forensic laboratories were analysed by OHID from the start of 2018 to the end of 2023 where xylazine was detected are summarised in Table 2 below by year of detection.

Table 2. Xylazine detections in from 2018 to end of Q3 2023.

Substance		Cases/detections					
	2018	2019	2020	2021	2022	2023	Total
Xylazine	0	0	0	1	0	1	2
Medetomidine	0	0	0	0	0	0	0
Detomidine	0	0	0	0	0	0	0
Grand Total	**0**	**0**	**0**	**1**	**0**	**1**	**2**

TICTAC Communications Ltd.

10.12. TICTAC Communications Ltd. is a leading provider of drug identification and drug information to the criminal justice and healthcare sectors. It is based at St. George's University of London and for over 25 years it has provided drug identification products, services and analysis to a wide range of organisations including police forces, the Home Office, prisons, customs, forensic laboratories, DAATs, hospitals, universities, pharmacies, pharmaceutical companies and suppliers of pharmacy dispensing systems.

10.13. In September 2023, TICTAC Communications Ltd. analysed two blotters from eight seized in August 2023 at a South of England musical festival and both GC-MS and QTOF analysis identified that they contained a combination of xylazine and fluoroexetamine (an NPS from the arylcyclohexylamine family of drugs, which is thought to have dissociative effects similar to ketamine).

10.14. There have been no other products analysed that have contained xylazine. No products analysed to date by TICTAC Communications Ltd. have contained detomidine or medetomidine.

National Poisons Information Service (NPIS)

10.15. The NPIS is commissioned by the UK Health Protection Agency to provide poisons information and clinical advice to UK health professionals managing patients who may have been exposed to potentially toxic substances, including drugs of misuse. For most cases information is provided via an internet database (TOXBASE); this received almost 3 million substance enquires in the year 2021-22 via its online and TOXBASE app platforms. When TOXBASE cannot be accessed or for more complex cases a 24/7 telephone enquiry line is available with consultant support, and this received almost 40,000 health professional enquiries during the 2021-22 reporting year. Numbers of accesses to TOXBASE and NPIS telephone enquiries reflect (but do not measure directly) the frequency of contacts between health professionals and patients presenting following suspected exposures.

10.16. There have previously been very few telephone enquiries to the NPIS related to xylazine (1 call in 2019) and medetomidine (1 call in 2019 and 1 in 2020) and no calls related to detomidine. No further information is available on the circumstances of use, the clinical features experienced or the outcome for the patients involved.

10.17. Online and app TOXBASE accesses for xylazine, medetomidine and detomidine are summarised in the Table 3 below. It should be noted that as these are all licensed veterinary medicines, it is not possible to know whether these accesses related to accidental or intended (including recreational) human exposures to the compounds. The sharp increase in online TOXBASE xylazine accesses in 2023 may reflect health professionals seeking general information in response to increasing publicity about xylazine, as opposed to reflecting increased patient contacts.

Table 3. TOXBASE accesses for xylazine, medetomidine and detomidine.

	2018	2019	2020	2021	2022	2023
Xylazine						
TOXBASE online	4	3	6	2	1	188
TOXBASE app	0	2	0	1	8	50
Medetomidine						
TOXBASE online	23	26	7	22	33	24
TOXBASE app	2	1	1	3	2	0
Detomidine						
TOXBASE online	10	19	14	15	14	13
TOXBASE app	5	5	1	1	3	0

Identification Of Novel psychoactive substances (IONA) study

10.18. The IONA study collected and analysed biological (blood and/or urine) samples from consenting patients attending over 30 participating EDs in England, Wales and Scotland after illicit drug use between May 2015 and March 2023.

10.19. During this period samples from a total of 1,815 patients were analysed, including 323 where heroin and 5 where fentanyl was recorded as a suspected exposure. None of the samples analysed were found to contain xylazine, medetomidine or detomidine. It is worth noting that the laboratory conducting the analyses has been able to detect these 3 compounds in other forensic samples.

European Drug Emergencies Network Plus (Euro-DEN Plus) project: UK Centres

10.20. The European Drug Emergencies Network (Euro-DEN) was established in 2013 with European Union funding. After the first year of data collection, it was expanded as the Euro-DEN Plus project, with ongoing support from the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). The project collects data on presentations with acute drug toxicity related to the use of recreational drugs, novel psychoactive substances and recreationally used prescription and over the counter medicines to sentinel EDs/toxicology units across Europe. It should be noted that the majority of Euro-DEN Plus

cases are based on self-reported use of drugs used, rather than analytical confirmation, and therefore the possibility of xylazine being used with heroin may not be identified.

10.21. Between October 2013 and December 2022 there were 15,589 presentations to the sentinel UK EDs in the Euro-DEN Plus project. There were no reported cases of acute toxicity related to reported use of xylazine, medetomidine or detomidine in these UK presentations.

Deaths in the UK related to xylazine, medetomidine and detomidine

10.22. Following contact with all forensic and toxicology laboratories in the UK, there is evidence of xylazine detections in biological samples from sixteen persons (eleven fatal, two non-fatal, three with outcome details redacted– ten from July/August 2023 alone) (Table 3). Whilst in most cases xylazine was detected in biological samples along with heroin and fentanyl – a common combination in the USA – this polydrug use pattern is not evident in all cases, suggesting a wider circulation of xylazine in the illicit drug market beyond heroin supplies. In addition, it is not possible to determine whether it was the heroin and/or fentanyl that contained the xylazine that was detected, rather than it having been in any of the other drugs used.

10.23. It should be noted that widespread screening for xylazine was only added by forensic and toxicology laboratories from June 2023 onwards after widespread reporting in May 2023 of the death in Birmingham in May 2022. In Table 4 below, cases 2 and 5 were identified by retrospective screening of biological samples once the coroner and/or laboratory were aware of the possibility of xylazine being involved in deaths in the UK.

Table 4. Xylazine detections in biological samples in the UK (May 2022-August 2023).

Case #	Date	Location	Case Type	Co-detected drugs
1	May 2022	Birmingham	Fatal	Alcohol, cannabis, cocaine, diazepam, diphenhydramine, fentanyl, heroin, methadone, paracetamol, pregabalin
2	December 2022	Lincolnshire	Fatal	Amphetamine, caffeine, clomipramine, cocaine, codeine, cyclizine, naloxone, quetiapine
3	February 2023	Wiltshire	Fatal	Alcohol, amphetamine, aripiprazole, bromazolam, cocaine, codeine, fluoxetine, heroin, mitragynine, quetiapine, methadone
4	March 2023	Hampshire	Fatal	Cocaine (as benzoylecgonine), heroin,

				methadone, pregabalin, promethazine
5	April 2023	Berkshire	Fatal	Caffeine, cocaine, fentanyl, heroin, mirtazapine, naloxone, paracetamol, pregabalin, quetiapine, venlafaxine
6	June 2023	Birmingham	Non-Fatal	Alfentanil*, cocaine, cyclizine, heroin, ketamine*, methadone, ondansetron*, paracetamol, pregabalin, tranexamic acid*
7	July 2023	Birmingham	Fatal	N-ethylpentylone or N,N-dimethylpentylone
8	July 2023	Birmingham	Fatal	N-desethyl isotonitazene
9	July 2023	Glasgow	Non-Fatal	Bromazolam, heroin, metonitazene, protonitazene, paracetamol, sertraline,
10	August 2023	Birmingham	Fatal	Cocaine, heroin, N-desethyl isotonitazene
11	August 2023	[Redacted]	Fatal	[Redacted]
12	August 2023	[Redacted]	Fatal	[Redacted]
13	August 2023	Glasgow	Fatal	Metonitazene, protonitazene
14	July/August 2023	[Redacted]	[Redacted]	[Redacted]
15	July/August 2023	[Redacted]	[Redacted]	[Redacted]
16	July/August 2023	[Redacted]	[Redacted]	[Redacted]

*Indicates administered as part of medical treatment.

11. Conclusions

11.1. Xylazine, detomidine and medetomidine are prescription veterinary medicines with legitimate uses in a variety of different animal species as sedatives and/or pre-medications prior to use of alternative injectable or inhalational anaesthetics. There are no legitimate uses of these compounds in humans, although dexmedetomidine, the active isomer of medetomidine, is licensed for use in humans as a sedative for those in intensive care units or undergoing diagnostic or surgical procedures.

11.2. Information on the acute toxicity of these compounds is largely from intentional and/or accidental exposure in legitimate veterinary practice. It appears that these compounds predominately cause sedation which is unresponsive to naloxone and may require intubation and admission to critical care.

11.3. Whilst there have been occasional international reports of misuse of detomidine and medetomidine, the ACMD has not been made aware of any evidence of misuse of these compounds in the UK. Currently the risks of health or social harms from the misuse of either of these two compounds in the UK appear small and no further action is warranted at present.

11.4. Xylazine has been very commonly detected as an adulterant and/or associated with illicit opioids such as fentanyl in North America. It is thought to be added to illicitly synthesised fentanyl to increase and/or prolong the sedative effects of the fentanyl (which are shorter than those of heroin), possibly in part by reducing the metabolism of fentanyl.

11.5. In the UK to date there is little evidence that individuals are actively seeking to use xylazine. The compound has only been detected in a very small number of analysed samples in which fentanyl has not been co-detected. Instead these samples positive for xylazine have also contained cannabis, benzodiazepines and/or other opioids such as tramadol or codeine. With the reduction in the availability of heroin from Afghanistan, however, there may be an increase in the use of illicitly synthesised fentanyls in the UK opioid market, with the potential for increasing use of xylazine as an enhancer or extender.

11.6. It is unclear from the literature whether the co-use of illicit opioids with xylazine is associated with more severe toxicity than that seen with the illicit opioids alone. However, xylazine is expected to increase the severity and duration of sedation and respiratory depression caused by opioids. The sedative effects associated with xylazine, if used recreationally and/or administered to an individual with malicious intent, could potentially put an individual at risk of accidents or crimes such as assault, robbery or sexual assault. In addition, there are anecdotal and published reports of significant skin ulceration related to the injection of drugs containing xylazine.

11.7. Dependence and associated withdrawal in individuals thought to be using illicit opioids containing xylazine has been described, although it is unclear whether

the features seen in those individuals relates to use of xylazine or illicit opioids.

11.8. Xylazine has been detected in a number of deaths in the UK. It is not clear whether the increase in the number of deaths where it has been detected reflects increased use or more widespread screening for the compound. In all cases, a range of other drugs were detected including classical and novel opioids, stimulants (cocaine, amphetamine), benzodiazepines and other sedatives (pregabalin, diphenhydramine ketamine). The contribution of the detected xylazine to the cause of the reported deaths is currently unclear.

11.9. Because of the recent increase in the numbers of detections in the UK, the likelihood of further increases in its prevalence and the potential health and social harms associated with xylazine, the ACMD advises that control of xylazine via the Misuse of Drugs Act 1971 is necessary. Harms are considered to be broadly equivalent to those of other sedatives such as benzodiazepines, zopiclone or pregabalin, so listing in Class C is recommended.

11.10. The ACMD does not wish to hamper the legitimate use of xylazine in veterinary medicine and recognises the lack of evidence of diversion of veterinary supplies to the illicit drug market. For this reason, listing in Schedule 4 Part 1 of the Misuse of Drugs Regulations is recommended, as this does not require Controlled Drug prescription requirements, safe custody arrangements and drug registers.

12. Recommendations

Recommendation 1.
Although there is no evidence of intended use of xylazine at this time in the UK, given the acute toxicity of xylazine and the similarity to the enhanced toxicity seen when benzodiazepines are co-used with opioids, xylazine should be added to Class C of the Misuse of Drugs Act 1971.

As xylazine has legitimate use as a veterinary medicine, it should be placed in Schedule 4 Part 1 of the Misuse of Drugs Regulations 2001 (as amended).

Lead: Home Office.

Measure of outcome: The inclusion of the listed compounds in Class C of the Misuse of Drugs Act 1971 and Schedule 4 Part 1 of the Misuse of Drugs Regulations 2001.

Recommendation 2.
Information should be provided in an appropriate format to the general public (such as FRANK) and to harm reduction services on the potential that heroin, fentanyl and other illicit drugs may contain xylazine. This should include information on the potential health effects, including the potential for ulceration associated with the injection of xylazine.

Leads: UK Health Security Agency, Office for Health Improvement and Disparities.

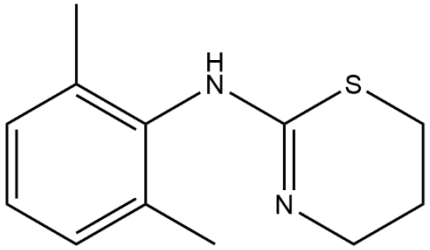
Measure of outcome: Information available for the general public, including those with lived experience.

Recommendation 3.
Responsible agencies need to be vigilant and monitor for substances, such as xylazine and related compounds such as detomidine and medetomidine that might be used to augment the opioid market in the UK. This can be done by analysis of seized or submitted drug samples (especially seized heroin and other opioid samples) and analysis of patient toxicology and post mortem samples. These data can then be collected, collated and monitored by the relevant public health agencies in the UK and reviewed by the newly established Synthetic Opioid Taskforce.

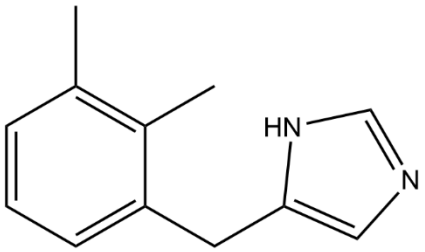
Leads: Office for Health Improvement and Disparities, Public Health Wales, Public Health Scotland, Public Health Agency Northern Ireland, Synthetic Opioid Taskforce

Measure of outcome: Information on substances used to augment the UK opioid market provided to the ACMD by the Synthetic Opioid Taskforce.

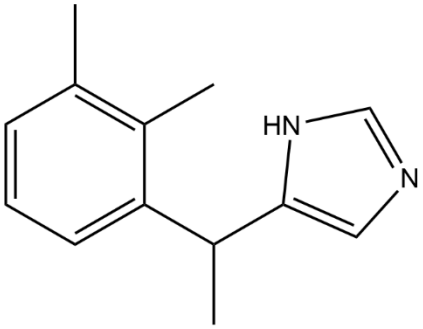
Annex A: The chemical structures for xylazine, medetomidine and detomidine, along with clonidine and lefoxidine



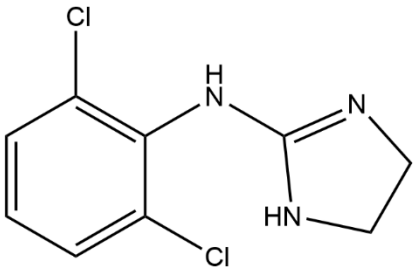
Xylazine



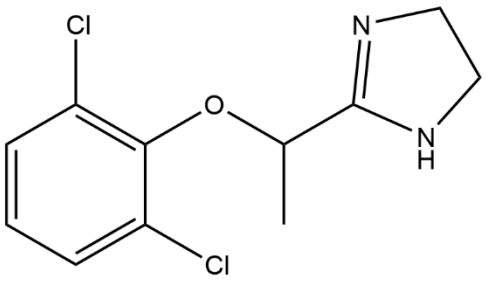
Detomidine



Medetomidine



Clonidine



Lofexidine

Annex B: Chair and Members of ACMD Xylazine, Medetomidine and Detomidine working group

Chair of Working Group	
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
Members of Working Group	
Dr Gabrielle Casha*	Pharmaceuticals Efficacy Assessor, Veterinary Medicine Directorate
Dr Caroline Copeland*	Lecturer in Pharmaceutical Medicine at King's College London, and the Director of the National Programme on Substance Abuse Deaths
Mr John Corkery*	Senior Lecturer in Pharmacy Practice at University of Hertfordshire; mortality and epidemiological lead for EU-MADNESS project
Dr Hilary Hamnett	Associate Professor in Forensic Science, University of Lincoln
Professor Graeme Henderson	Professor of pharmacology at the University of Bristol
Professor Chelsea Shover*	Assistant Professor-in-Residence, UCLA David Geffen School of Medicine, USA
Professor David Taylor	Professor of psychopharmacology, King's College, London
Professor Simon Thomas	NPS Committee Chair, Emeritus Professor of Clinical Pharmacology and Therapeutics, Newcastle University
Mr Ric Treble*	Retired Laboratory of the Government Chemist (LGC) expert

*denotes co-opted member of the ACMD working group

Annex C: ACMD Novel Psychoactive Substances Committee membership, at time of publication

Dr Kostas Agath	**Consultant psychiatrist (addictions), Change Grow Live Southwark**
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**	Lecturer in Pharmaceutical Medicine at King's College London, and the Director of the National Programme on Substance Abuse Deaths
Mr John Corkery**	Senior Lecturer in Pharmacy Practice at University of Hertfordshire; mortality and epidemiological lead for EU-MADNESS project
Mr Lawrence Gibbons	Head of drug threat – National Crime Agency Intelligence Directorate – Commodities
Dr Hilary Hamnett	Associate Professor in Forensic Science, University of Lincoln
Professor Graeme Henderson	Professor of Pharmacology at the University of Bristol
Professor Stephen Husbands**	Professor of Medicinal Chemistry, University of Bath
Professor Roger Knaggs	Associate Professor in clinical pharmacy practice at the University of Nottingham
Professor Fiona Measham**	Professor and chair in criminology at the University of Liverpool; co-founder and co-director, the Loop
Mr Harry Shapiro	Director – DrugWise
Dr Richard Stevenson	Emergency Medicine Consultant, Glasgow Royal Infirmary

Dr Ann Sullivan	Consultant physician in HIV and sexual health, Chelsea and Westminster Hospital NHS Foundation Trust
Professor Simon Thomas	NPS Committee Chair, Emeritus Professor of Clinical Pharmacology and Therapeutics, Newcastle University
Mr Ric Treble**	Retired Laboratory of the Government Chemist (LGC) expert
Dr Derek Tracy	Medical director of West London NHS Trust
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

**denotes co-opted member of ACMD Novel Psychoactive Substances Committee

Annex D: ACMD membership at the time of publication

Dr Kostas Agath	Consultant psychiatrist (addictions), Change Grow Live Southwark
Professor Judith Aldridge	Professor of criminology at the 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
Dr Anne Campbell	Reader in substance use and mental health and co-director of the Drug and Alcohol Research Network at Queens University Belfast
Dr Emily Finch	Clinical director of the Addictions Clinical Academic Group and a consultant psychiatrist for South London and Maudsley NHS Trust
Mr Mohammed Fessal	Chief pharmacist, Change Grow Live
Mr Lawrence Gibbons	Head of drug threat at the National Crime Agency Intelligence Directorate – Commodities
Dr Hilary Hamnett	Associate Professor in forensic science at the University of Lincoln
Professor Graeme Henderson	Professor of pharmacology at the University of Bristol
Dr Carole Hunter	Lead pharmacist at the alcohol and drug recovery services at NHS Greater Glasgow and Clyde
Professor Roger Knaggs	Associate professor in clinical pharmacy practice at the University of Nottingham
Mr Harry Shapiro	Director – DrugWise
Dr Richard Stevenson	Emergency medicine consultant, Glasgow Royal Infirmary
Dr Paul Stokes	Reader in mood disorders and psychopharmacology, King's College, London

Dr Ann Sullivan	Consultant physician in HIV and sexual health, Chelsea and Westminster Hospital NHS Foundation Trust
Professor David Taylor	Professor of psychopharmacology, King's College, London and Director of Pharmacy and Pathology at the South London and Maudsley NHS Foundation Trust
Professor Simon Thomas	Emeritus professor of clinical pharmacology and therapeutics, Newcastle University
Dr Derek Tracy	Medical director of West London NHS Trust
Ms Rosalie Weetman	Public health lead (alcohol, drugs and tobacco), Derbyshire County Council - (currently on secondment to Office for Health Improvement and Disparities, as 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

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