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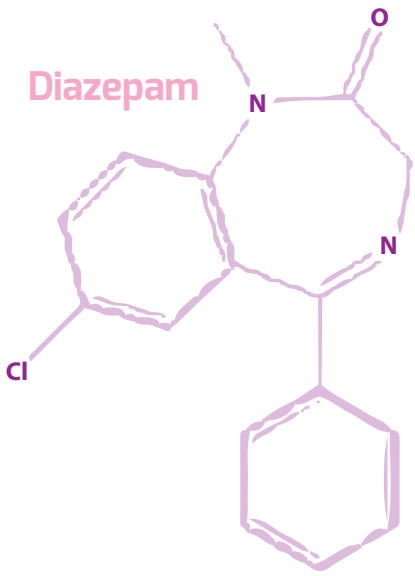
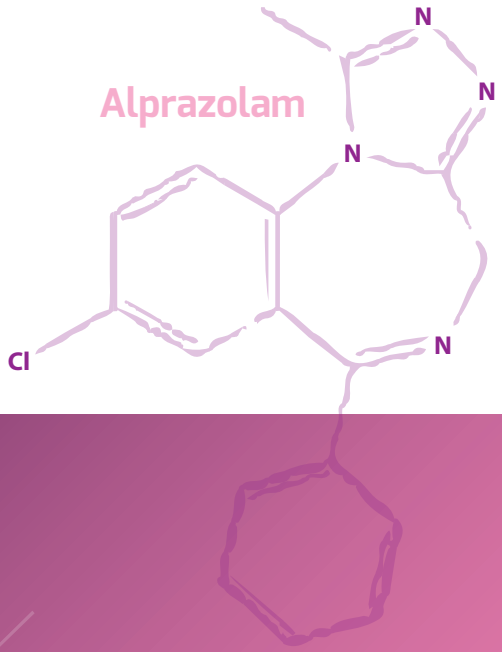
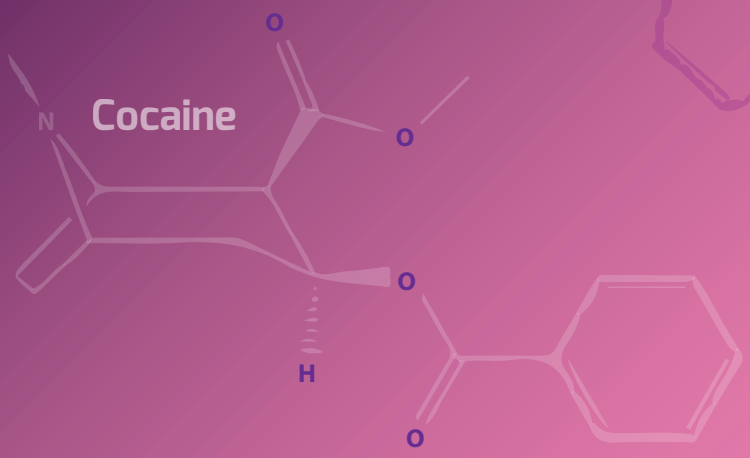
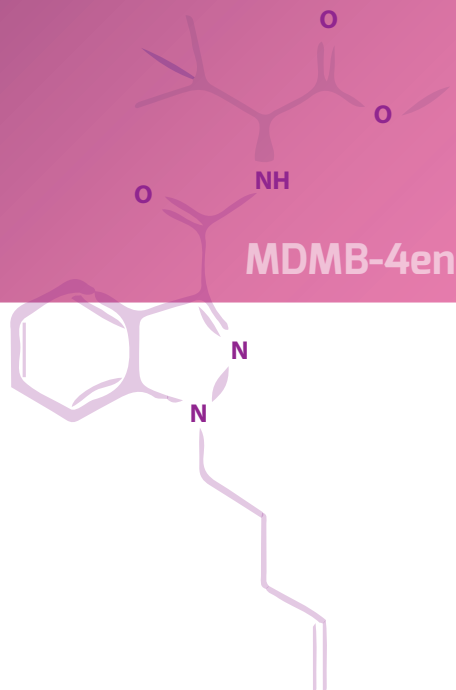
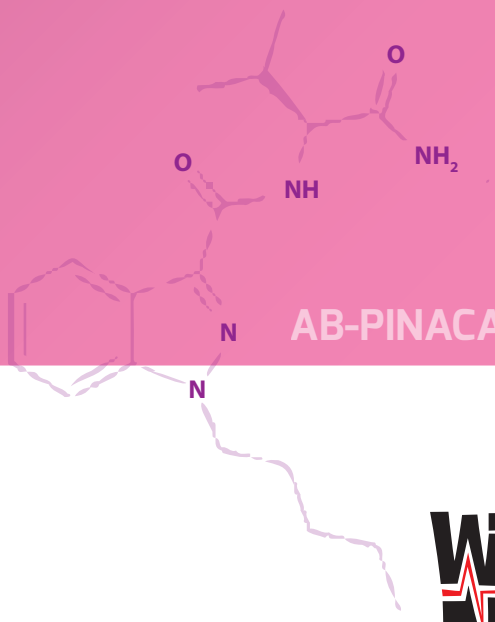




Annual Report
Adroddiad Blynyddol
2020 - 2021







WEDINOS

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Foreword

Whilst this last year has been extraordinary in so many ways, the work of WEDINOS has continued unabated, so sincere thanks go to the WEDINOS laboratory team, project management and all those individuals and organisations who continued to submit samples and support the ongoing work of the programme.

Despite COVID, we have not seen substantial impact on drug markets or on types of samples submitted for analysis, with the exception of those received via night time economy settings. In the absence of samples from night club amnesty bins and other recreational use settings, we have seen a decline in ketamine, cocaine and other stimulants for profiling.

For the fourth consecutive year, the most commonly identified chemical group of psychoactive substances were benzodiazepines. With 18 different benzodiazepines identified compared to 13 identified in 2019/20 and high levels of substitution, either partial or total, of other benzodiazepines.

The purchase of non-prescribed and non-controlled benzodiazepines, generally obtained through an online market, is a growing concern. Many of the benzodiazepine tablets available on illicit markets are not of pharmaceutical grade, but are in fact counterfeit. This is of public health concern as these counterfeit products may contain varying amounts of the active ingredients, substituted drugs with different onset and duration periods, different strengths or combinations of substances making it hard for individuals to make decisions regarding dosage and to reduce potential harms associated with use. As a consequence, the risk of adverse effects, development of dependency, hospitalisation or death are increased, particularly when alcohol and/or other drugs are taken alongside or within a short period.

WEDINOS remains a vital service and, once again, thanks to all that support this programme and we look forward to responding to the new challenges as lockdowns ease.

Josie Smith
Head of Substance Misuse, Public Health Wales

WEDINOS - a reminder

WEDINOS is funded by Welsh Government and was launched in October 2013 as a collaboration between Public Health Wales, Cardiff Toxicology Laboratories at University Hospital Llandough, Cardiff and Vale University Health Board and the School of Pharmacy at Cardiff University.

WEDINOS provides a framework for the collection and testing of samples of psychoactive substances and combinations of drugs (hereafter referred to as "samples") along with information on the symptoms that those submitting samples experienced, both expected and unexpected. Collation of these findings along with identification of the chemical structure of the samples enables the dissemination of pragmatic evidence-based harm reduction information for those using psychoactive drugs or considering use.

The analytical tools used for the profiling of samples includes a Quadrupole Time of Flight (Q-ToF) mass spectrometer (the primary analytical tool), a Fourier-Transform Infrared (FTIR) spectrometer, Nuclear Magnetic Resonance (NMR) spectroscopy, Gas Chromatography–Mass Spectrometry (GC-MS) and Liquid Chromatography–Mass Spectrometry (LC-MS).

Headline Figures 2020/21

Total to date:

19,829 samples received

- 16,904 analysed
- 460 substances identified either in isolation of combination.
- from 207 different organisations, services and night time economy (NTE) venues (night club amnesty bins) from across the UK.

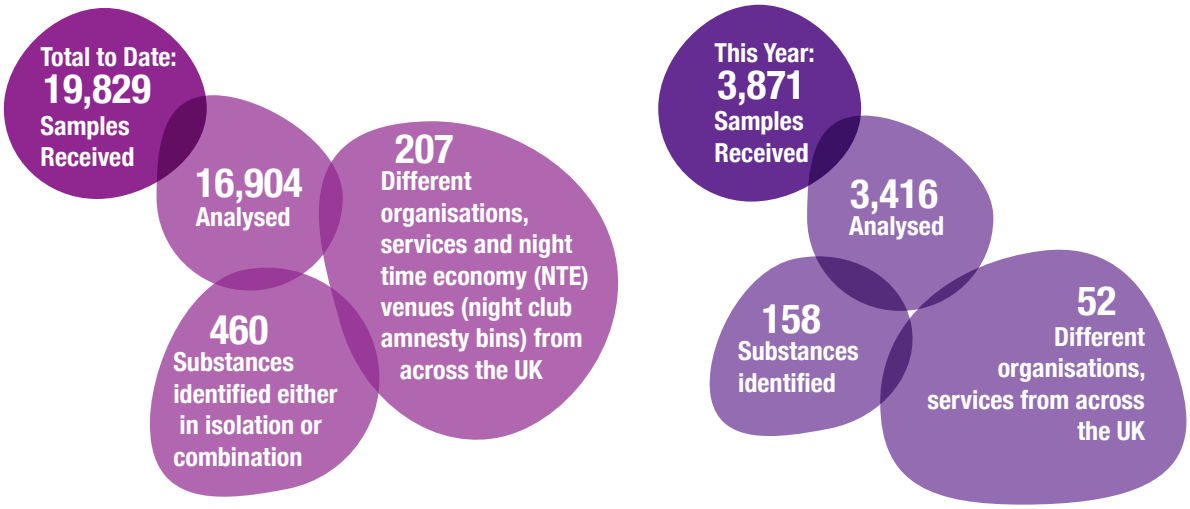
This Year 2020/21:

- 3,871 samples received representing a decrease ▼ 21 per cent due to zero submissions from NTE venues following Covid restrictions.
- 3,416 analysed ▼ down 16 per cent overall.
  - Community samples increased ▲ 28 per cent.
- 158 substances identified ▼ down 7 per cent.
- Samples received from 52 different organisations, services a decrease ▼ 42 per cent.
- Median age of sample providers 33 years (range 14 to 89 years) of age.
- As in the previous three years, benzodiazepines were the most commonly identified class of mind altering / psychoactive substances.
- For the first year, diazepam was the most commonly identified substance within all samples recieved, due to the absence of NTE samples. In previous years, cocaine has consistently been the most commonly identified substance.
  - Most commonly identified in the community - diazepam, followed by cocaine.
  - Within criminal justice settings, most commonly identified substance – MDMB-4en-PINACA, followed by buprenorphine and nicotine.

benzodiazepines

diazepam

Fig. 1: WEDINOS activity to date and in last year 2020/21



Wider Perspective . . .

Global, European, England and Wales, and Welsh estimates:

At a global level, The United Nations Office for Drugs and Crime (UNODC) estimates that in 2018, 269 million people, or 5.3 per cent of the population aged 15 to 64 had used drugs in the previous year. This includes an estimated 11.3 million people who inject drugs. An estimated 35.6 million people who use drugs (51.6 per cent) required treatment services.

585,000
people died as a result of drug use

In 2017, 585,000 people died as a result of drug use globally. More than half of those deaths were the result of untreated hepatitis C leading to liver cancer and cirrhosis; almost one third were attributed to drug use disorders. Two thirds of the deaths attributed to drug use disorders were related to opioid use.[1.]

Within the European Union, the European Monitoring Council for Drugs and Drug Addiction (EMCDDA), reported that an estimated 96 million people* or 29 per cent of the population aged 15-64 had tried illicit drugs in their lifetime.[2.]

In the United Kingdom, the Crime Survey for England and Wales (CSEW) 2019/20 reported that 3.2 million people, or 9.4 per cent of adults aged 16-59, had taken a drug in the last year, the same as that estimated for 2018/19. Around 21 per cent of 16-24 year olds reported taking a drug in the last year, and for adults aged 60-74, 1 per cent reported using drugs in the last year, consistent with previous years.[3.]

1. World Drug Report 2020 (United Nations publication, Sales No. E.20.XI.6) https://wdr.unodc.org/wdr2020/index.html [accessed 29th April 2021]. 2018 is the most recent data available.
2. European Monitoring Centre for Drugs and Drug Addiction (2020), European Drug Report 2020: Trends and Developments, Publications Office of the European Union, Luxembourg https://www.emcdda.europa.eu/publications/edr/trends-developments/2020_en [accessed 29th April 2021].
3. Crime Survey for England and Wales 2019/20; Drug misuse in England and Wales: year ending March 2020. https://www.ons.gov.uk/peoplepopulationandcommunity/crimeandjustice/articles/drugmisuseinenglandandwales/yearendingmarch2020 [accessed 29th April 2021].

* This should be regarded as a minimum estimate due to reporting biases.

** In this context problem drug use (PDU) is defined by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) as "injecting drug use or long duration or regular use of opioids, cocaine and/or amphetamines [including amphetamine type substances]".

Harms from Substance Use - Wales

In Wales, the overall number of hospital admissions for poisonings with named illicit drugs has decreased by 9.4 per cent in the last year, from 6,714 in 2018-19 to 6,081 in 2019-20. Compared to 2015-16 there has been a 2.7 per cent decrease in illicit drug admissions.[4.]

240
Deaths

In 2019, 240 deaths due to drug poisoning were registered in Wales, a decrease of 27 per cent from the previous calendar year. Of the drug-poisoning deaths, 69 per cent were defined as a drug misuse death, specifically drug deaths involving illicit drugs controlled under the Misuse of Drugs Act 1971 and other related legislation. [5., 6.]

WEDINOS . . . Samples

3,416
Samples

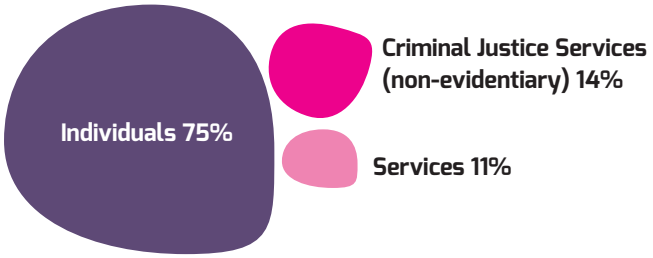
In 2020-21 WEDINOS received and analysed 3,416 samples from 52 services and settings across the UK, as well as from individuals. These samples can be separated into two broad categories:

- Community
- Criminal Justice Settings

Samples submitted under the category 'Criminal Justice Settings' include non-attributable finds from within criminal justice settings including prisons in Wales. As such, these samples are not accompanied by any information relating to purchase intent, effects or demographics. During 2020-21, no samples were received from night time economy (NTE) settings, e.g. night club amnesty bins, due to COVID-19 restrictions.

Samples submitted under the category 'Community' include samples submitted via organisations and services, or by individuals.

Source of samples submitted to WEDINOS



4. Public Health Wales (2021), Data Mining: The annual profile for substance misuse 2019-20 https://phw.nhs.wales/publications/publications1/data-mining-wales-the-annual-profile-for-substance-misuse-2019-20/ (accessed 29th April 2021).
5. A death where the underlying cause is either drug abuse or drug dependence, or the underlying cause is drug poisoning and any of the substances controlled under the Misuse of Drugs Act 1971 are involved.
6. Public Health Wales (2020), Drug related mortality for deaths registered in 2019.

Key Findings . . . What . . .

Most commonly identified substances – All samples

benzodiazepines

The most commonly identified chemical group of psychoactive substances, for the fourth consecutive year, were benzodiazepines. 18 benzodiazepines were identified compared to 13 identified in 2019/20, however, six were identified on five or less occasions.

diazepam
flubromazolam

As with the previous three year's findings, **diazepam** (n=377) was the most commonly identified benzodiazepine. Diazepam was identified in 13 per cent of all community samples received. **Flubromazolam** was the second most commonly identified substance, with 255 identifications, despite it being reported only once as a purchase intent. Flubromazolam is most commonly identified as a substitute for diazepam, but also within samples submitted as alprazolam. Flubromazolam is more potent than both diazepam and alprazolam. This is a potential risk for individuals using benzodiazepines as dosage and potency varies greatly.

For the first time since project launch (2013) cocaine was not the most commonly identified psychoactive substance identified. This is likely as a result of the lack of samples from the NTE during this reporting period.

Evidence from the EMCDDA reported the highest number and quantity of cocaine seizures, and an increase in cocaine purity year on year in their most recent report. There was also little evidence from the EMCDDA of disruption to dark web purchases of cocaine, this is particularly pertinent as the United Kingdom plays a key part in darknet market.[7]

Chart 1: Increases in cocaine submissions to WEDINOS are evident at points of COVID-19 restriction easing in England and Wales during 2020.

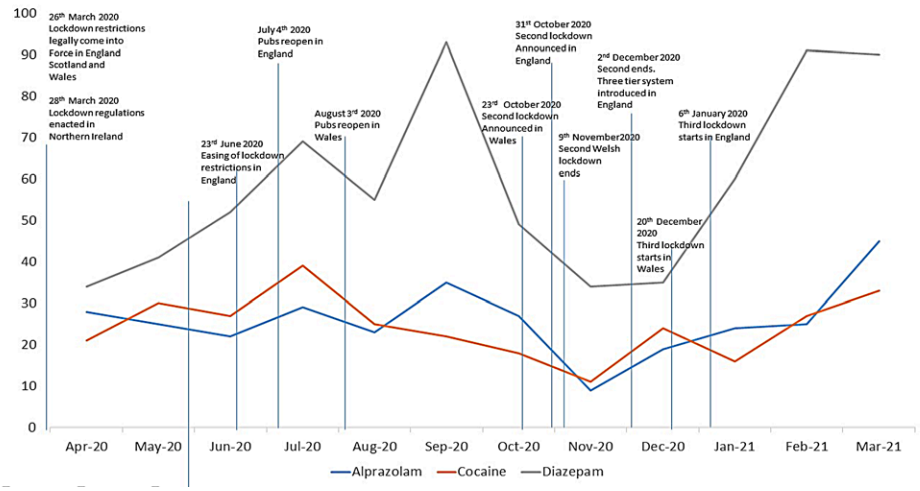


Chart 1 above shows increases in cocaine submissions to WEDINOS are evident at points of COVID-19 restriction easing in England and Wales during 2020-21. This may evidence a trend of increased social/recreational use during these periods.

7. European Monitoring Centre for Drugs and Drug Addiction (2020), European Drug Report 2020: Trends and Developments, Publications Office of the European Union, Luxembourg https://www.emcdda.europa.eu/publications/edr/trends-developments/2020_en [accessed 29th April 2021].

The CSEW 2019/20 reported no change in last year self-reported use of cocaine, among adults aged 16 to 59. However, the CSEW did report a fall in the number of frequent users from 14.4% in year ending March 2019 to 8.7% in year ending March 2020.

Consistent with previous years, caffeine was the most popular bulking/cutting agent identified, however, as well as being found in combination with other substances, several samples of powders and tablets were found to contain caffeine in isolation.

Table 1: Most commonly identified mind altering/psychoactive substance WEDINOS samples.

	2020/21	2019/20
1	Diazepam	Cocaine
2	Cocaine	MDMA
3	Flubromazolam	Diazepam
4	Etizolam	Ketamine
5	MDMB-4en-PINACA	Etizolam
6	Flualprazolam	Caffeine
7	Alprazolam	4F-MDMB-BINACA
8	MDMA	Cannabis
9	Caffeine	Flualprazolam
10	Tetrahydrocannabinol	Alprazolam

In the next section of this report, we focus on samples from community settings. WEDINOS works closely with the six Welsh prisons, reporting separately on finds with no evidentiary value.

Community Settings . . .

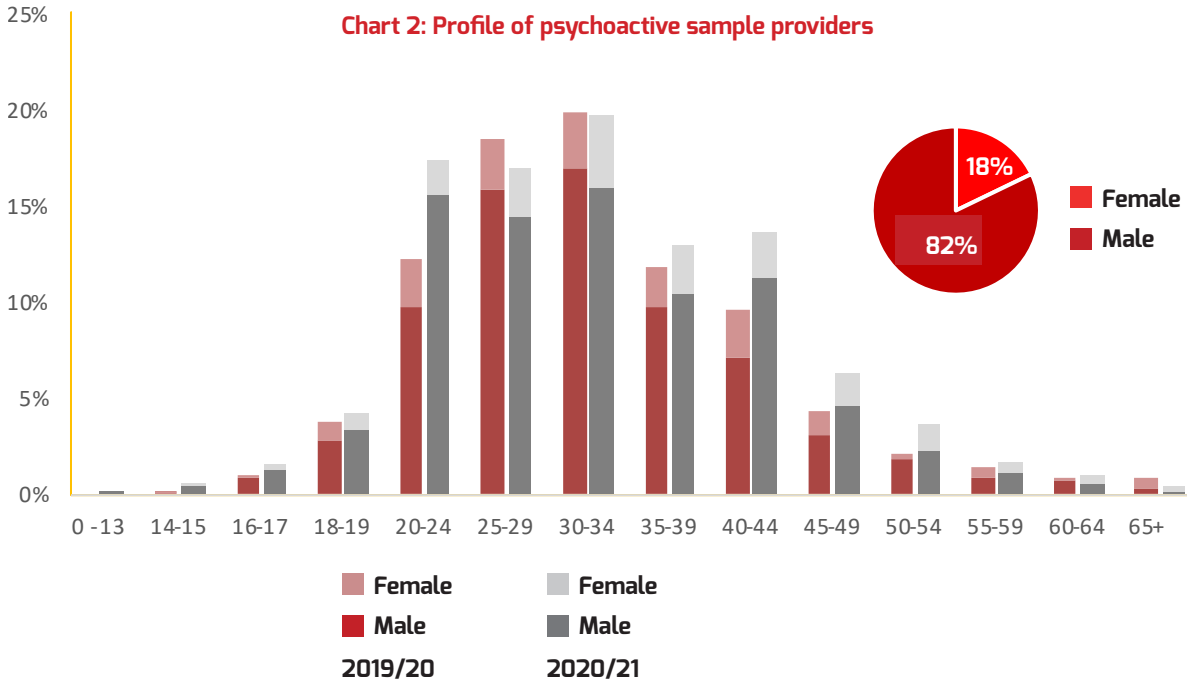
During 2020-21 a total of 2,936 samples were submitted from community settings including education, health (incl. emergency departments), mental health, housing and homelessness, substance misuse services as well as from individuals. Of these 2,936 samples, demographic information was available for 90 per cent (n=2,629).

82 per cent of the samples were submitted by males and 18 per cent by females. This is the same as last year.

The median age for all mind altering / psychoactive sample providers (Wales and wider UK) was 33 years of age, range 14 to 89 years, in comparison to 32 years and 12 to 80 years in 2019-2020.

- Females - median age was 34 years (35 years in 2019-2020) (range: 14-73 years).
- Males - median age was 32 years (31 years in 2019-2020) (range 14-89 years).

Chart 2: Profile of psychoactive sample providers



Samples submitted by individuals aged 0-17 years, included (in order of prevelance):

- flubromazolam (all purchased as diazepam)
- flualprazolam (all purchased as alprazolam)
- ketamine
- cannabis
- zopiclone
- LSD
- MDMA
- Temazepam
- 2C-B
- 4F-MDMB-BINACA and AB-PINACA (both purchased as cannabis vape liquids).

For older adults, aged 60 years and above, samples submitted contained:

- Amphetamine
- Cocaine
- descloroetizolam (all purchased as diazepam)
- diazepam
- diclazepam (purchased as diazepam)
- etizolam
- flubromazolam (all purchased as diazepam)
- zopiclone
- mephedrone
- cannabis
- methamphetamine

Community Samples: What . . .

Since the launch of WEDINOS in 2013 the project has consistently evidenced the substitution of substances within the UK's illicit drug market. Table 2 shows the changes in the "top 10 most common" substances at the submission stage (purchase intent) and the post analysis.

Samples listed as "unknown" include samples submitted under a name that does not allow the substance or category of substance to be identified. In addition, there are a number of samples found or containing unknown substances, including those submitted by patients with acute effects within a health setting, such as an emergency department or mental health ward.

Table 2: Most common substances pre (perceived) and post (actual) analysis

	Community purchase intent	Community post analysis
1	Diazepam	Diazepam
2	Alprazolam	Cocaine
3	Cocaine	Flubromazolam
4	Unknown	Etizolam
5	MDMA	Alprazolam
6	THC Vape Liquid	Flualprazolam
7	Ketamine	MDMA
8	Amphetamine	Caffeine
9	Zopiclone	No Active Component Identified
10	Mephedrone	Ketamine

Table 2 profiles the differences between the most commonly reported substances pre-analysis; and the most commonly identified contents post-analysis.

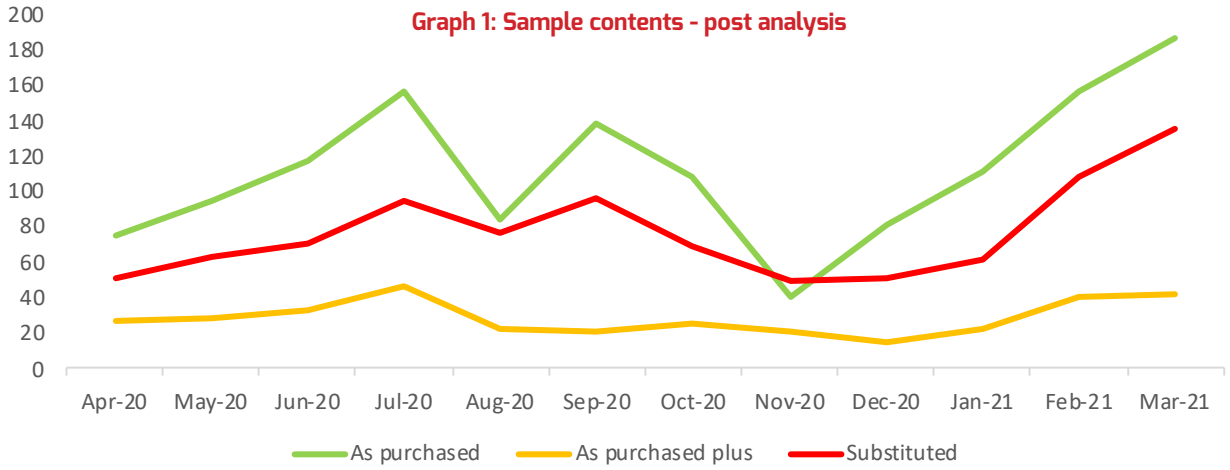
Of particular importance is the finding that Flubromazolam, etizolam and flualprazolam are not present on the pre-analysis list, however, sit as the third, fourth and sixth most identified substances overall. All three substances were listed a total of 44 times in the pre-analysis purchase intent. However, following analysis these substances were identified in a total of 618 samples.

It may be argued that the high pre-analysis presence of "unknown" substances would be the biggest influencer of this change, however, after removal of these samples it was found that over the past year 35 per cent of samples submitted to WEDINOS with a substance listed in the purchase intent did not contain what was expected, compared to 42 per cent in 2019-2020.

Some samples were found to contain the purchase intent plus additional substances, such as a sample purchased as MDMA, upon analysis was found to contain MDMA and cocaine. Other samples were found to contain a different substance or substances from the purchase intent, for example a sample purchased as alprazolam, which was found to contain flualprazolam, etizolam and flubromazepam.

The levels of additional substances and substitutions are shown in Graph 1.

Graph 1: Sample contents - post analysis



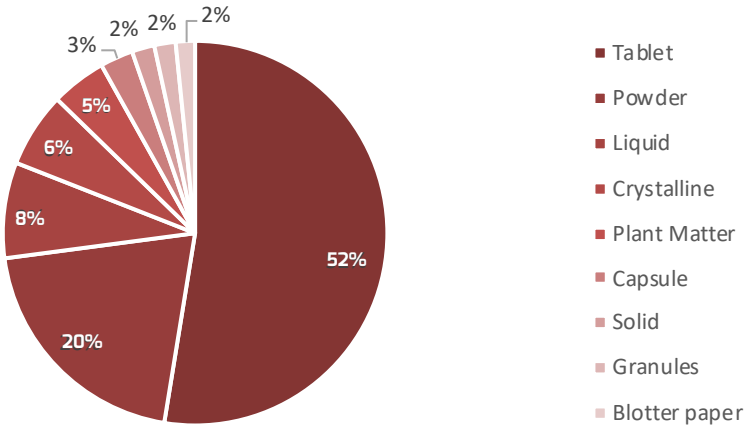
Graph 1: Profile of samples submitted to WEDINOS 2020-21 identifying 'as purchased', 'as purchased' plus additional substances and samples substituted with other substances, based on stated purchase intent.

Community: How . . .

Form of sample

WEDINOS requests the 'form of sample' for each submission to monitor and report the various forms substances appear on the market and potential differences in method of consumption.

Chart 3: Form of psychoactive samples



As in the previous year, we have seen a continued increase in the proportion of tablets submitted. This is mirrored by the increase in submissions believed to diazepam and alprazolam and these samples / substances are usually found in tablet form.

Method of Consumption and Harm Reduction Advice

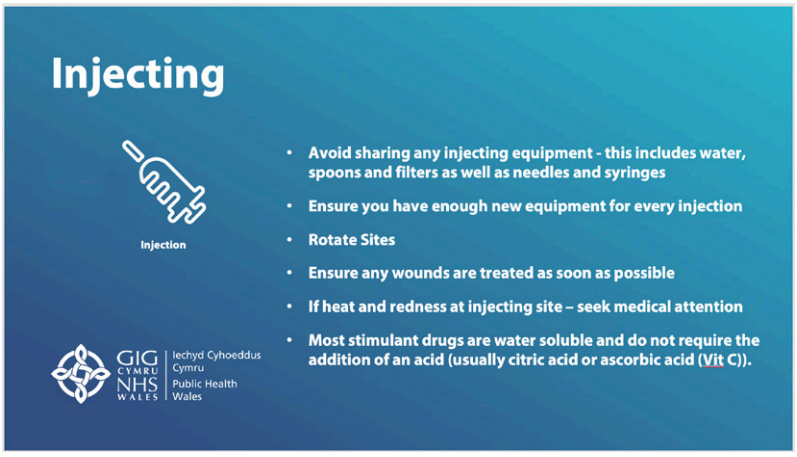
Assuming that all plant matter samples are smoked, the remaining samples (pills, liquids, tabs, granules, etc.) were ingested through a variety of methods, with 71 per cent taken orally (swallowing, bombing), up from 69 per cent in 2019-2020. A further 18 per cent reported snorting / sniffing the substance, a decrease from 23 per cent in 2019-2020, as shown in Chart 4. Increased oral consumption in the community is evidenced through increased samples of tablets being submitted to WEDINOS.

Chart 4: Method of Consumption

One per cent reported intravenous injecting of substances.

Samples injected were purchased as and found to contain, heroin amphetamine, and fentanyl.

Injecting drug use carries with it inherent risks of bacterial and viral infection over and above the risks / toxicity of the substance being injected.



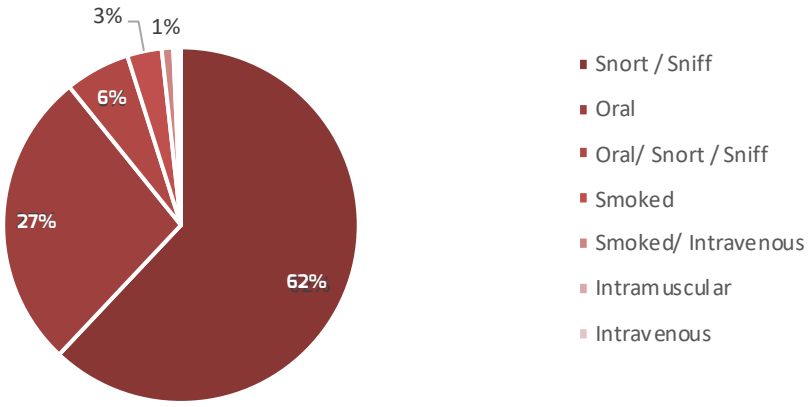
For further harm reduction information, please visit:
http://www.wedinos.org/harm_reduction_advice.html

All injecting, regardless of the substance, carries a significant risk of serious infection and other implications. Individuals who currently inject drugs or have previously injected should get tested for blood borne viruses.

Powders and crystalline materials

Focusing on the method of use for, powders and crystalline materials the most common method of consumption was snorting/sniffing with 62 per cent reporting this as shown in Chart 5, this is camparable to 2019-2020.

Chart 5: Method of consumption: Powders



Snorting/sniffing caustic or toxic substances risks causing damage to the nasal passages which increases the risk of blood borne viral infection transmission when sharing snorting paraphernalia.

Benzodiazepines

Benzodiazepines (sometimes called "benzos") calm or sedate a person, they act at benzodiazepine receptors which are associated with gamma-aminobutyric acid (GABA). Generally they are known as a group of pharmaceutical substances, prescribed for anxiety and sleep disorders, and are the most commonly used anxiolytics (sedatives) and hypnotics.[8.]

Benzodiazepines include substances such as diazepam (Valium) and temazepam, which are prescribed as medicines in the UK. Other benzodiazepines are not licenced or generally prescribed in the UK, such as alprazolam (Xanax) and etizolam, but are prescribed in other countries such as Italy, India and Japan.

During the reporting period 2020-2021 WEDINOS received 1,205 samples submitted, with purchase intent indicated, as benzodiazepines.

WEDINOS does not currently collate data relating to sample source, however, we are aware that benzodiazepines of all kinds are available in the illegal drugs market. Some may be diverted or obtained from those receiving a prescription, although the majority are purchased as illegal drugs and are generally referred to as "street valium". Street valium can contain a range of unlicensed medicines and substitute substances, which will be evidenced later in this section.[9.]

In 2020-21 Diazepam was the most commonly identified substance in samples submitted to WEDINOS and there may be several reasons for this. Firstly, there are reports of a reduced demand for substances typically used in social settings,[10.] such as the night time economy, that were closed in the UK as a result of national COVID-19 restrictions. Secondly, there were reports of increased interest in other substances, and the appearance of benzodiazepines on the New Psychoactive Substances market.[11.] In addition, the United Nations Office for Drugs and Crime (UNODC) reported an increase in the use of pharmaceutical products such as benzodiazepines[12.]. Furthermore, internationally UNODC theorised that opioid shortages caused by COVID-19 restrictions could lead to users substituting with more readily available substances such as alcohol or benzodiazepines, or to mixing with synthetic drugs[11.] potentially increasing the prevalence of diazepam. However, personal correspondence with drug services and harm reduction leads across Wales does not substantiate this hypothesis as many areas reported no significant disturbance to the Welsh heroin market, as described by service users. Despite the relative stability of the Welsh heroin market, all areas of Wales reported an increase in benzodiazepine use.

8. Hypnotics and anxiolytics, National Institute for Health and Care Excellence, 2021; https://bnf.nice.org.uk/treatment-summary/hypnotics-and-anxiolytics.html [accessed 13th May 2021].
9. Benzodiazepines (benzos, diazepam, valium), NHS Inform, https://www.nhsinform.scot/healthy-living/drugs-and-drug-use/common-drugs/benzodiazepines-benzos-diazepam-valium [accessed 13th May 2021].
10. European Monitoring Centre for Drugs and Drug Addiction (2020), European Drug Report 2020: Trends and Developments, Publications Office of the European Union, Luxembourg https://www.emcdda.europa.eu/publications/edr/trends-developments/2020_en [accessed 29th April 2021].
11. European Monitoring Centre for Drugs and Drug Addiction and Europol (2020), EU Drug Markets: Impact of COVID-19, Publications Office of the European Union, Luxembourg. https://www.emcdda.europa.eu/system/files/publications/13097/EU-Drug-Markets_Covid19-impact_final.pdf [accessed 13th May 2021].
12. United Nations Office for Drugs and Crime (2020), World Drug Report 2020; https://wdr.unodc.org/wdr2020/index.html [accessed 13th May 2021].

Benzodiazepines featured as number 10 in the top 20 substances most commonly used by respondents to the Global Drug Survey 2020, rising to number 7 when alcohol and nicotine/tobacco products were excluded.[13.] *

Benzodiazepines accounted for the majority of illicit drugs seized, measured by dose, in England and Wales, with over 719,000 doses seized in 2019-20, up from 212,000 doses seized in 2018-19. This is over a 200 per cent increase. 84 per cent of all benzodiazepine doses seized in England and Wales were seized in Wales.[14.]

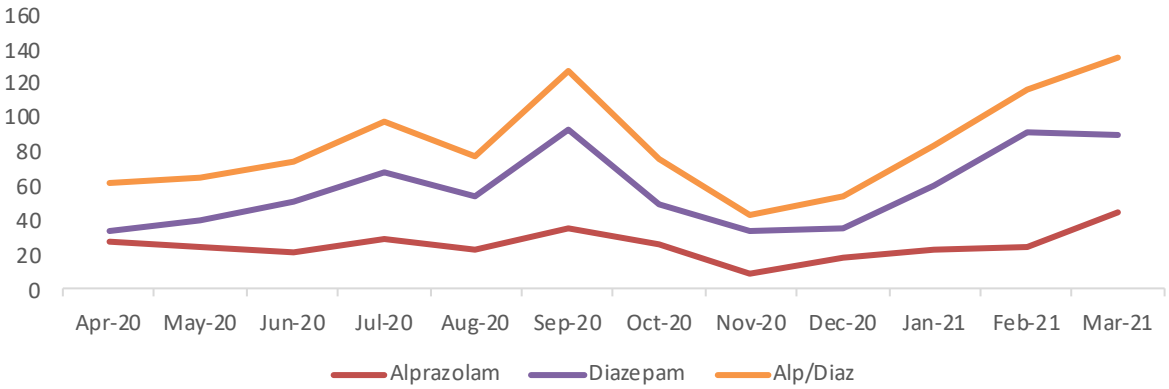
The purchase of non-prescribed and non-controlled benzodiazepines, generally obtained through an online market, is a growing concern.[10.] Many of the benzodiazepine tablets available on illicit markets are not of pharmaceutical grade, but are in fact counterfeit.[15.] This is of public health concern as these counterfeit products may contain varying amounts of the active ingredients, substituted drugs with different onset and duration periods, different strengths or combinations of substances making it hard for individuals to make decisions regarding dosage and to reduce potential harms associated with use.

WEDINOS analysis of counterfeit alprazolam has identified the samples to contain other drugs and/or potentially dangerous adulterants (see ****). This finding is not limited to alprazolam due to the growing presence of online pharmacies. While some online pharmacies are legitimate, others are not and may either be scam or provide drugs of uncertain origin, uncertain drug type, or inconsistent dosing.[16.]

The benzodiazepines most commonly submitted to WEDINOS, based on sample provider self-reported purchase intent, were diazepam and alprazolam.

13. GDS2020 Key Findings Report:Executive Summary, 2021. https://www.globaldrugsurvey.com/wp-content/uploads/2021/01/GDS2020-Executive-Summary.pdf [accessed 13th May 2021].
* GLOBAL DRUG SURVEY 2020 (GDS2020). Data from over 110,000 people from over 25 countries.
14. Public Health Wales (2020), Data mining Wales: The annual profile for substance misuse 2019-20. https://phw.nhs.wales/publications/publications1/data-mining-wales-the-annual-profile-for-substance-misuse-2019-20/ [accessed 13th May 2021].
15. Lyphout, C., Yates, C., Margolin, Z. et al. Presentations to the emergency department with non-medical use of benzodiazepines and Z-drugs: profiling and relation to sales data. Eur J Clin Pharmacol 75, 77–85 (2019). https://doi.org/10.1007/s00228-018-2550-1
16. Kelsie Watkins, O. Hayden Griffin & Elizabeth A. Gardner (2019) Investigation of black box drugs purchased from an online pharmacy, Journal of Substance Use, 24:4, 445-449, DOI: 10.1080/14659891.2019.1595197

Graph 2: Monthly submissions of samples purchased as alprazolam and diazepam to WEDINOS 2020-2021



diazepam

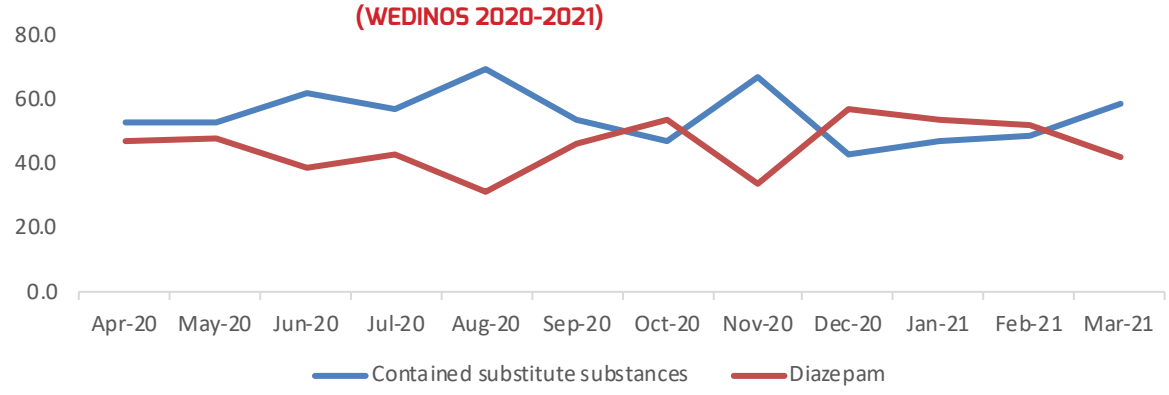
Diazepam:
Diazepam is the generic name of compound 1, which was originally manufactured by Hoffman-La Roche as Valium. First synthesized in 1959, diazepam entered the pharmaceutical market in 1963.

alprazolam

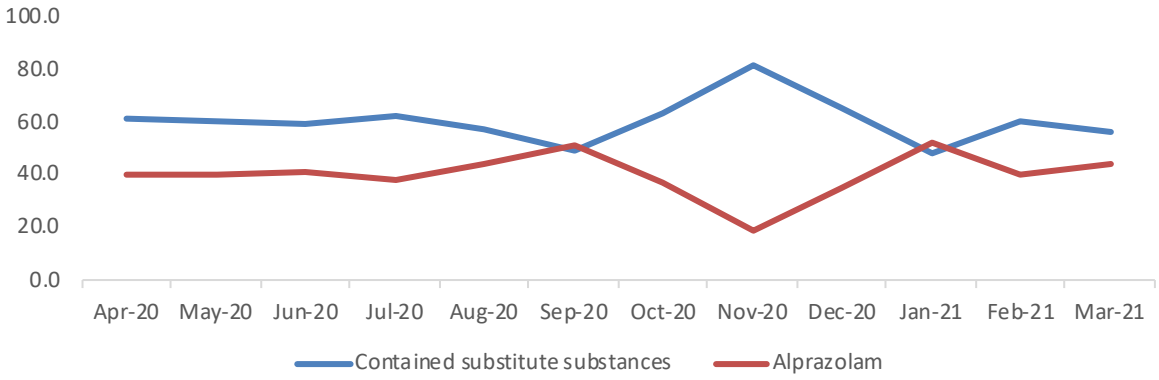
Alprazolam:
Alprazolam was patented in the 1970s, developed at Upjohn Company (later part of Pfizer, Inc.). In 1981 it was approved by the U.S. Food and Drug Administration (FDA) for treatment of anxiety or from panic disorder. Alprazolam tablets are not prescribable in NHS primary care.

In the WEDINOS 2019-2020 report evidence was provided for significant substitution amongst samples purchased as diazepam (47 per cent) and alprazolam (65 per cent). Throughout 2020-2021, WEDINOS has continued to evidence the substitution of benzodiazepines with other substances.

Graph 3: Post analytical content of samples submitted as diazepam (WEDINOS 2020-2021)

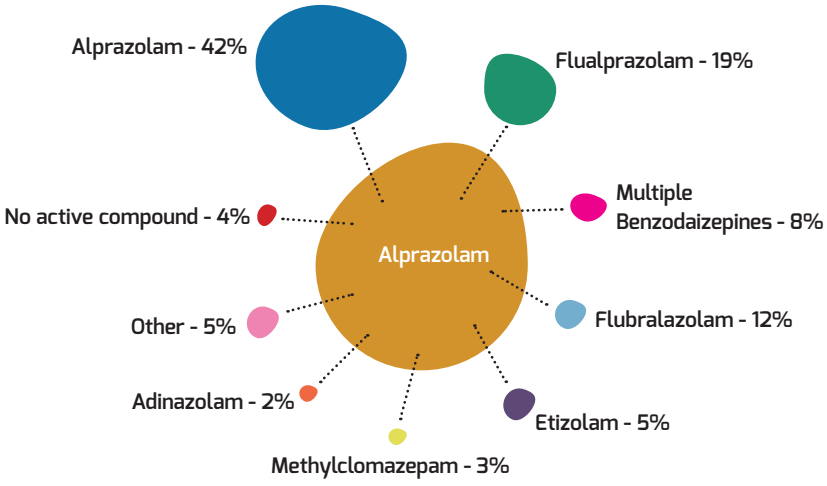


Graph 4: Post analytical content of samples submitted as alprazolam (WEDINOS 2020-2021)

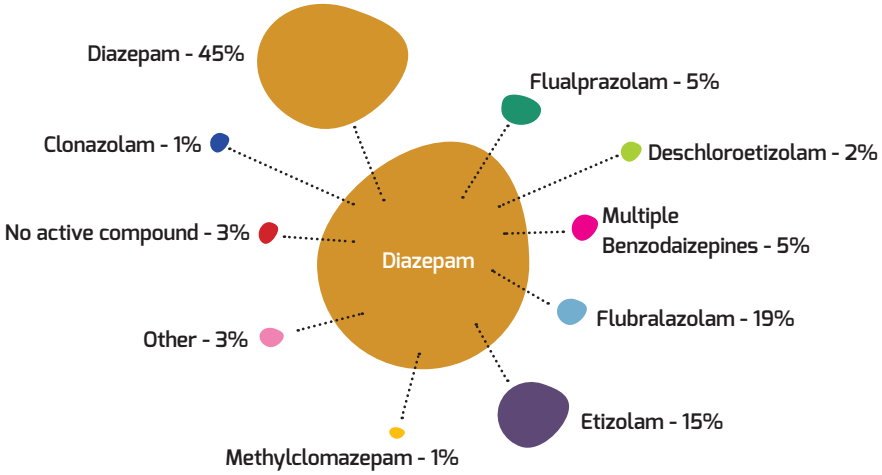


In 2020-21:

- 712 samples were submitted to WEDINOS with purchase intent stated as diazepam, within which 22 other substances, either in isolation or combination, were identified
- Of the 320 samples submitted as alprazolam 16 other substances, either in isolation or combination, were identified. 58 per cent of samples submitted as alprazolam were found to contain other substances. The most common substitute was flualprazolam. See diagram below.



For diazepam the rate of substitution was 55 per cent, with the most common substitute being flubromazolam. See diagram below.



flualprazolam

Flualprazolam

Flualprazolam a triazolo-benzodiazepine, similar to triazolam and alprazolam and structurally different from benzodiazepines such as diazepam. It was first patented in the 1970's but was never marketed.

Flualprazolam has sedative effects similar to other benzodiazepines. It is a higher potency benzodiazepine with relatively short onset of action[17].

flubromazolam

Flubromazolam

An example of this substitution of diazepam with flubromazolam is shown here. Following analysis using Liquid Chromatography Quadrupole Time-of-Flight accurate mass spectrometry (UPLC/QToF) this sample submitted as diazepam was found to contain the benzodiazepine **Flubromazolam**.

Flubromazolam is a substituted benzodiazepine, which is structurally related to pyrazolam. The substance has been researched in the patent literature for its anxiolytic properties and sedative, hypnotic, and ataxic side effects, but it is not licensed for medicinal use (European Information System and Database on New Drugs).

It is incredibly potent (active in the microgram range) with an unusually long 18-hour duration.[18]

17. World Health Organisation, Critical review report: Flualprazolam, 2019; https://www.who.int/medicines/access/controlled-substances/Final_Flualprazolam.pdf?ua=1 [accessed 13th March 2021].
18. https://psychonautwiki.org/wiki/Flubromazolam

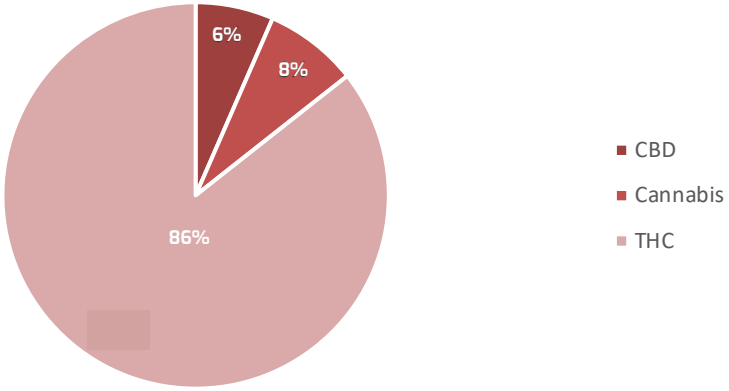
E-liquids / C-liquids/Vapes

Vape pens / e-cigarettes are devices that allow the user to inhale a substance in a vapour rather than smoke.[19] They work by heating a liquid that, in terms of WEDINOS results, typically contains one or a combination of the following substances: nicotine, cannabidiol (CBD), tetrahydrocannabinol (THC), cannabinol (CBN) or Synthetic Cannabinoid Receptor Agonists (SCRAs).

In 2020-2021, WEDINOS received 194 samples submitted in liquid form for use with a vape pen. Purchase intent was listed for 79 per cent (n=153) of these samples, the remaining 21 per cent (n=41) were submitted as "vape liquid".

Where a substance was named in the purchase intent, all samples were related to cannabis, either named as cannabis, CBD or THC.

Chart 6: Purchase intent (where reported) for samples submitted as vape liquids to WEDINOS 2020-2021



Of serious concern is the finding that of the 153 samples submitted with stated purchase intent, 56 per cent (n=85) were found to contain SCRAs. In addition, a further 6 samples, reported in purchase intent as 'vape liquids', also contained SCRAs. Therefore 46 per cent of all samples submitted to WEDINOS 2020-21 as vape liquids contained SCRAs.

Within the 91 vape liquid samples found to contain SCRAs, four substances were identified either in isolation or combination: MDMB-4en-PINACA (n=47), AB-PINACA (n=36), 4F-MDMB-BINACA (n=22) and 5F-ADB (n=1).

19. Using e-cigarettes to stop smoking-Quit smoking, NHS, https://www.nhs.uk/live-well/quit-smoking/using-e-cigarettes-to-stop-smoking/ [accessed 13th May 2021].

MDMB-4en-PINACA was subject to an EMCDDA risk assessment in March 2021. There is limited information on the pharmacological properties of MDMB-4en-PINACA. It is a full agonist of the CB1 receptor, and has high potency. "Adverse effects from overdosing MDMB-4en-PINACA might include gastrointestinal (e.g. nausea and vomiting (including hyperemesis)), neurological (e.g. hallucination, seizures, convulsions, agitation, anxiety, paranoia, confusion, delusions, catatonia, lethargy, psychosis (including susceptible individuals) and severe central nervous system depression (such as rapid loss of consciousness/coma), cardiovascular (e.g. tachycardia, hypertension, acute myocardial infarction and sudden cardiac death) and renal (e.g. acute kidney failure) clinical features, and respiratory depression".

With respect to smoking mixtures and vape liquids, MDMB-4en-PINACA consumed in this way is rapidly absorbed into the blood stream. This alongside the high potency of this SCRA makes it difficult for individuals to control their dosage. Reports relating to fatal and non-fatal poisonings describe severe effects and fatal poisonings from a small number of puffs. The UK reported 11 confirmed non-fatal poisonings as a result of MDMB-4en-PINACA between January and August 2020.

The term 'synthetic cannabinoids' covers all synthetic substances that bind to one of the two known cannabinoid receptors (CB1 or CB2).[20.]

Most SCRAs have higher affinities for the CB1 receptor than tetrahydrocannabinol (THC) and are full agonists of this site. THC in comparison acts as a partial agonist.[21.]

In their 2014 report, the European Monitoring Council for Drugs and Drug Addiction stated '**that these substances can be extremely potent, but are not chemically similar to cannabis, and therefore may result in different and potentially more serious health consequences. Although our current understanding of the health implications of consuming these substances remains limited, there is increasing concern about reports of acute adverse consequences associated with their use**'.[22].

In the WEDINOS annual report 2014-2015, some of the evidenced health harms relating to SCRAs were discussed, primarily concerns relating to psychosis. Where individuals were presenting with psychosis, these events were characterised by paranoid delusions, ideas of reference and a disorganised, confused mental state.[23.]

20. Auwärter V., Dargan P., Wood D., Novel Psychoactive Substances, Chapter 13 - Synthetic Cannabinoid Receptor Agonists, Academic Press, 2013,Pages 317-343, ISBN 9780124158160,https://doi.org/10.1016/B978-0-12-415816-0.00013-4.
21. WEDINOS annual report 2013-2014, Public Health Wales, Cardiff, 2014; https://www.wedinos.org/resources/downloads/WN%20Annual%20Report%205012015.pdf [accessed 13th May 2021].
22. European Monitoring Centre for Drugs and Drug Addiction (2014), European Drug Report 2014: Trends and Developments, Publications Office of the European Union, Luxembourg https://www.emcdda.europa.eu/publications/edr/trends-developments/2014_en [accessed 29th April 2021].
23. Abdulrahim D et al (NEPTUNE Expert Group).(2015). Guidance on the Management of Acute and Chronic Harms of Club Drugs and Novel Psychoactive Substances. Novel Psychoactive Treatment UK Network. London, NEPTUNE. Available at: http://neptune-clinical-guidance.co.uk/wp-content/uploads/2015/03/NEPTUNE-Guidance-March-2015.pdf [Accessed 13th May 2021]

SCRA products may cause more frequent and severe unexpected effects, with a relatively common occurrence of psychosis and psychosis-like symptoms amongst users. The presumption being that this is the result of the high potency and lack of CBD within SCRA products.[24.]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Youths hospitalised after being duped into vaping synthetic drug 'Spice'

The Public Health Agency (PHA) is urging parents to talk to their children about the dangers of being duped into vaping dangerous drugs by mistake over Easter.

By Philip Bradfield

https://www.newsletter.co.uk/health/youths-hospitalised-after-being-duped-into-vaping-synthetic-drug-spice-3188367

On 2 April 2021 the Public Health Agency (Northern Ireland) issued a Spice vaping warning following cases of young people falling ill after vaping SCRAs. Reports "suggested that those affected thought they were purchasing THC or cannabis oil, but they were unknowingly supplied with and had taken the synthetic drug 'spice', the effects of which required hospital treatment".[25.]

In the UK, two fatal drug poisonings relating to the vaping of SCRAs were described by Roberts et al[25.] from a retrospective look back at 42,000 deaths related to psychoactive drugs, other than nicotine or caffeine, which occurred between 1997 and 2020. Both deaths were associated with recent use of SCRAs, no other substances were found to be implicated in deaths. However, no details regarding the type of vaping products were available.[26.]

24. van Amsterdam J et al. (2015). The adverse health effects of synthetic cannabinoids with emphasis on psychosis-like effects. J Psychopharmacol 29(3):pp.254-63. doi: 10.1177/0269881114565142. Epub 2015 Jan 13.
25. Public Health Agency, Spice Vaping Warning Issued, April 2021, https://www.publichealth.hscni.net/news/spice-vaping-warning-issued-0 [accessed 13th May 2021].
26. Roberts, Emmert, et al. "Drug-related deaths associated with vaping product use in the United Kingdom." Addiction (2021).

GIG CYMRU NHS WALES
Iechyd Cyhoeddus Cymru
Public Health Wales

Llywodraeth Cymru
Welsh Government

Harm Reduction Wales
Lleihau Niwed Cymru