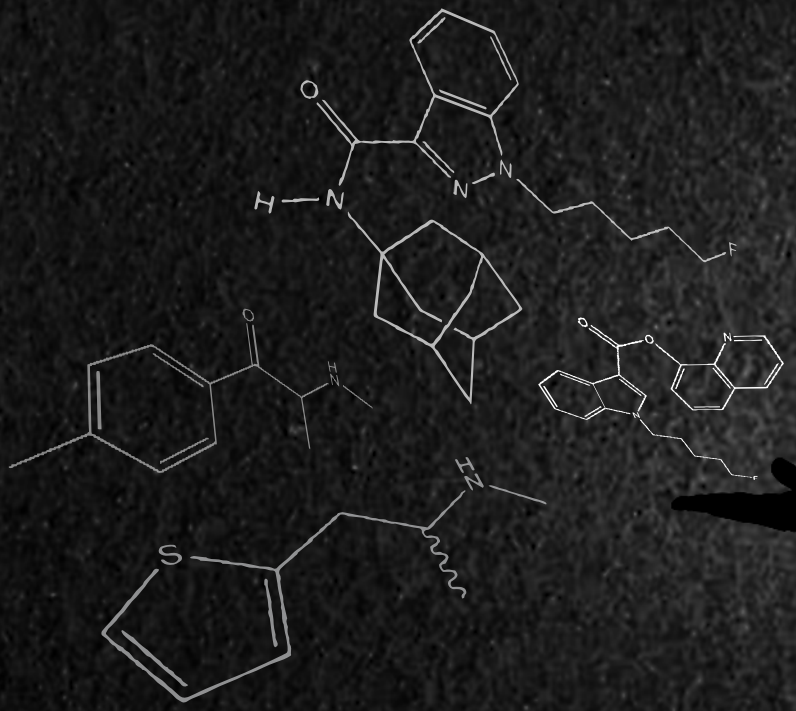
WEDINOS

PHILTRE

Annual Report

1st October 2014 - 30th September 2015



GIG CYMRU NHS WALES
Iechyd Cyhoeddus Cymru
Public Health Wales

Noddir gan
Lywodraeth Cymru
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Noddir gan Lywodraeth Cymru Sponsored by Welsh Government

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Foreword

"The last year has seen substantial increases, not only in the number of new psychoactive substances (NPS) and combinations of substances identified and in circulation but also in the harms experienced by those using them. Public Health are well placed to provide evidence on population trends in use, advise on how to reduce potential harms experienced by individuals and improve the care and support provided by health and social care professionals, frontline services and clinicians. WEDINOS fulfils this role and stands alone as an innovative project providing an evidenced, pragmatic and open approach to engagement with those using, considering use or affected by these drugs. This second annual report evidences a 25 per cent increase in NPS submissions on last year further reinforcing the vital role WEDINOS plays in this field."

Dr Marion Lyons
Director of Health Protection
Public Health Wales

HEADLINES

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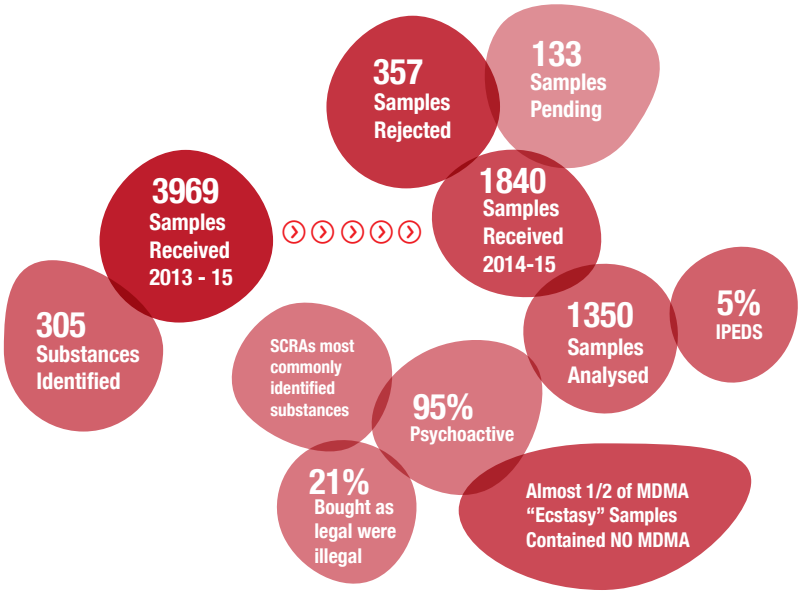


- WEDINOS provides a mechanism for the anonymous submission and testing of samples of new psychoactive substances and the dissemination of pragmatic harm reduction advice
- 1,350 samples analysed by WEDINOS*
- 305 compounds identified either in combination or isolation since project launch (September 2013)
- Median age for all mind altering/ psychoactive sample providers was 36 years
- 21 per cent of samples believed to be legal / not controlled contained a controlled compound
- 14 per cent of controlled samples contained a non-controlled NPS compound
- Synthetic Cannabinoid Receptor Agonists were the most commonly identified mind altering / psychoactive substances
- Of the 76 MDMA / Ecstasy samples - nearly half (n=35) did not contain MDMA
- 12 reporting forms submitted to the European Union Early Warning System (EWS)

*The total number of samples received by WEDINOS was 1,840. 357 samples were rejected based on our acceptance criteria. 133 samples had been received and were undergoing the analytical process at the time of writing.

REMINDER . . .

What are new psychoactive substances?

The term "new psychoactive substance" (NPS) has been legally defined by the European Union as a new narcotic or psychotropic drug, in pure form or in preparation, that is not scheduled under the Single Convention on Narcotic Drugs of 1961 or the Convention on Psychotropic Substances of 1971, but which may pose a public health threat comparable to that posed by substances listed in those conventions.[i]

New psychoactive substances are drugs which mimic, or are reported to mimic, the effects of illegal drugs. There is a common perception that because such drugs are legal they are safe. None of them, however, have been subjected to the stringent testing procedures which are required before a new medicine for human use is granted a license and, therefore, there is a risk of short and long-term adverse effects resulting from their use.

Substances categorized as NPS according to the United Nations Office on Drugs and Crime (UNODC) classification include:

- Synthetic cannabinoids
- Synthetic cathinones
- Phenethylamines
- Piperazines
- Ketamine
- Plant-based psychoactive substances such as kratom, *Salvia divinorum* and khat
- Other substances, including
  - Tryptamines
  - Aminoindanes
  - Phencyclidine-type substances.

Prevalence of NPS and contribution of WEDINOS to the international evidence base

The types and combinations of NPS are continually evolving and increasing. The European Union Early Warning System (EWS) provides a mechanism to inform and share information on trends and new substances, along with reported harms. The EWS is one of the activities of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). A record 101 new substances were reported to the EWS in 2014 (up from 81 in 2013), continuing an upward trend in substances notified in a single year. During the past year WEDINOS has submitted 12 reporting forms to the EU Early Warning System of substances that are a) new to reporting on a European level; b) new to reporting within the UK; c) causing concern. Specifically, these substances were identified from the following groups:

- Four synthetic cannabinoid receptor agonists (SCRA)
- Two piperidines & pyrrolidines
- One tryptamine
- One opioid
- One cathinone
- Two "others" (3F-Phenmetrazine and 1p-LSD)

There is very little evidence in terms of prevalence estimates for the use of NPS internationally. The Global Drugs Survey 2015 [ii], a self selecting survey, reported that 8.6 per cent of UK respondents to their survey declared the use of 'research chemicals / NPS use' in the last twelve months. This figure has fallen from 10.6 per cent in 2014 and 20 per cent in 2011.

i. Council Decision 2005/387/JHA of 10th May 2005 on the information exchange, risk-assessment and control of new psychoactive substances. OJEC L127/32; 48 (32). Available at: http://eur-lex.europa.eu/legal-content/en/ALL/?uri=CELEX:32005D0387 [Accessed 8th Dec 2015]
ii. Global Drugs Survey. (2015). The Global Drug Survey 2015 findings. Available at: http://www.globaldrugsurvey.com/the-global-drug-survey-2015-findings/ [Accessed 8th Dec 2015]

For the first time the 2014/15 Crime Survey for England and Wales (CSEW) [iii], a self report survey of England and Wales residents, included questions around the use of NPS among adults aged 16 to 59. For the context of the CSEW NPS relates to "newly available drugs that mimic the effect of drugs such as cannabis, ecstasy and powder cocaine, and which may or may not be illegal to buy, but are sometimes referred to as 'legal highs'".

Of respondents to the 2014/15 CSEW 0.9 per cent of adults aged 16 to 59 reported taking NPS in the last year, with 2.9 per cent stating that they had taken NPS at some point in their lifetime. For young adults, aged 16 to 24, 2.8 per cent had taken NPS in the last year; for males 16 to 24 this figure rose to 4 per cent.

In 2014, the Harm Reduction Database for Wales, which monitors activity throughout Welsh Needle & Syringe Programmes (NSP) began to capture NSP activity from community based pharmacy along with activity that it had already been recording from NSPs based within specialist statutory and voluntary services.

In NSPs based within specialist substance misuse services between 2011-12 and 2013-14, there was a substantial increase in individuals who declared NPS as their primary drug of choice; from 76 to 206, a rise of 171 per cent. In 2014-15, the figure was 206, however, with the inclusion of pharmacy NSP data this figure rises to 380.

The total number of those using NPSs, as either a primary or a secondary substance of choice has also increased in this period. In 2011-12, the total number of those accessing NSPs who reported NPS use was 152; in 2013-14 it was 351. In 2014-15, considering only figures from statutory or voluntary services, 406 individuals reported any use of NPS in the period, a rise of 15.7 per cent. When data from pharmacy based services are included, the number rises to 643.

As was stated in the 2013-14 report, this continued increase of NPS use as a secondary substance may indicate NPS being added more frequently to the drug use repertoire of Welsh individuals accessing NSPs. This is mirrored by the 2014/15 CSEW that found that young adults aged 16 to 24 who had used another substance in the last year were significantly more likely to have used an NPS in the last year (12.3 per cent) than those who had not (0.6 per cent). This difference is also statistically significant for the wider age group (16 to 59), and for most individual drug types.

NPS injecting (as a primary substance) as a proportion of all NSP activity in Wales within specialist statutory and voluntary services fell slightly from 2.3 per cent in 2013-14 to 2.1 per cent in 2014-15; however the number of individuals, 206, remained the same. Even following this decrease the proportion is still higher than the 1 per cent accessing statutory and voluntary service NSPs in 2011-12. As data collection from community pharmacy based NSPs only began in April 2014 we are unable to include comparisons of individuals attending those locations.

Samples Received

The continued success of WEDINOS to date has been achieved through active engagement with stakeholders. Over the past year, WEDINOS project staff have visited a number of settings including emergency departments, criminal justice services, housing and homelessness services and substance misuse use services providing training and guidance around NPS and WEDINOS.

iii. Home Office. (2015). Drug misuse: Findings from the 2014/15 Crime Survey for England and Wales 2nd ed. Statistical bulletin 03/2015. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/462885/drug-misuse-1415.pdf [Accessed 8th December 2015]

1st October 2014 to 30th September 2015

Between the launch of the project on 1st October 2013 and 30th September 2015, the WEDINOS project received 3,969 samples, identifying 305 substances either in isolation of combination. For the year October 2014 to September 2015, 1,350 samples were analysed, with 133 samples going through the analytical process. These samples were submitted by 53 different organisations and services from across Wales, an increase from 48 in 2013-14. Six services from across the wider UK also contributed this year.

Of the samples received from Wales 74 per cent were submitted through participating organisations and 26 per cent from individuals accessing via the website: **www.wedinos.org**.

Reason for Purchase

Of those 1,350 samples, 95 per cent were mind altering / psychoactive substances; the remaining 5 per cent being Image and Performance Enhancing Drugs (IPEDs). Over the past year the number of psychoactive samples analysed has increased by 25 per cent from 1,022 to 1,282.

As stated in the WEDINOS annual report 2013-14, on July 24th 2014 WEDINOS stopped accepting samples of IPEDs from the general public. However, samples can still be submitted via Public Health Wales approved and agreed sentinel providers to ensure contemporary evidence. This year 68 samples of IPEDs were submitted by the agreed sentinel providers, with samples originating from Wales, England and Scotland.

Mind altering/psychoactive substances – The Where, Who, What and How.

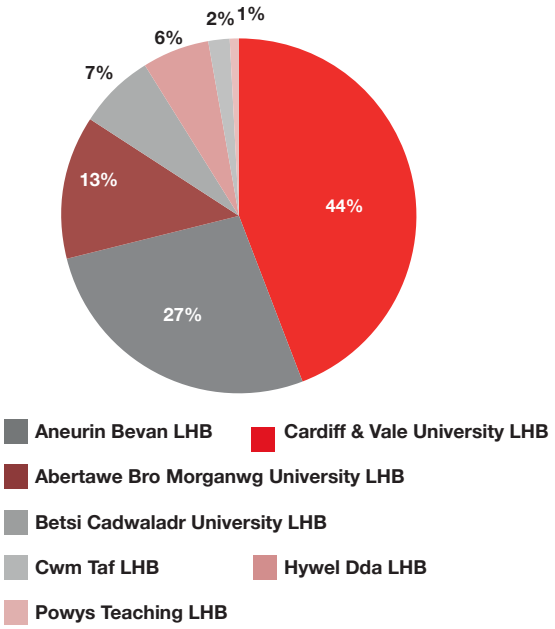
Of the 1,282 mind altering / psychoactive samples, 53 per cent were received from within Wales, 42 per cent from England, 2 per cent from Northern Ireland, 2 per cent from Scotland and the remaining 1 per cent was submitted from outside of the United Kingdom (the results of these analyses were not published).

Within Wales, the Cardiff and Vale University Local Health Board (LHB) area contributed the highest proportion of samples, accounting for 23 per cent of all mind altering/psychoactive samples and 43 per cent of Welsh submissions. Submissions from Cardiff and Vale University LHB area increased by 97 per cent from 150 submissions in 2013-14 to 295 this year.

Where ...

It should be noted that Chart 1 does not represent the spread, use or concentration of NPS use in Wales. It highlights the geographic variation in the engagement and proactive response of services with the WEDINOS project. South Wales Police and Gwent Police provide the WEDINOS project with substances that have been forfeited at night club amnesty bins. This enables the WEDINOS project to monitor trends in use amongst the club going population and to inform services within the locality of compounds in circulation.

Chart 1: Breakdown of Welsh submissions of mind altering / psychoactive samples by Local Health Board area



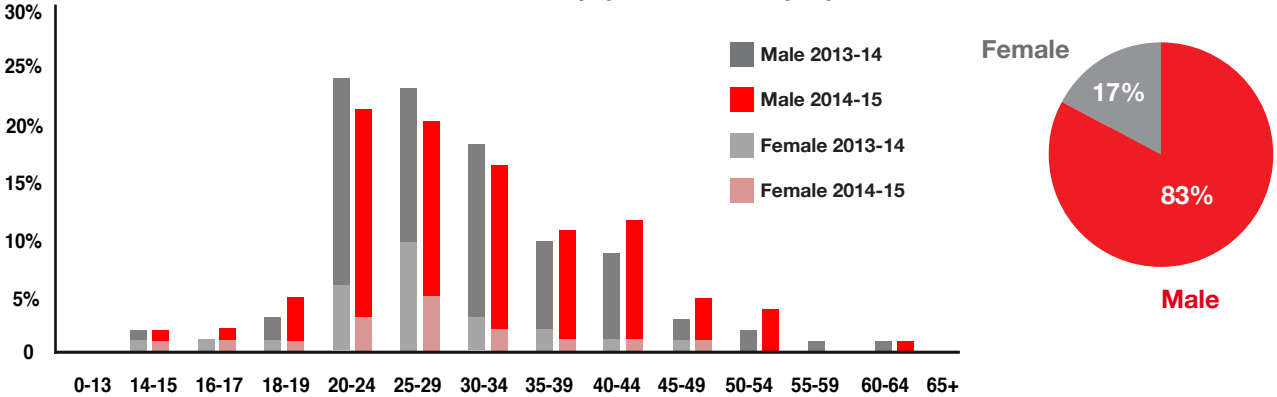
Who ...

Of the 1,282 samples, demographic information was available for 59 per cent (n=762), with the remaining samples submitted from amnesty bins or by criminal justice services and trading standards that had no evidentiary or forensic value, hence with no self-report effects form. 83 per cent of the samples were submitted by males and 17 per cent by females, as shown in Chart 2.

The overall median age for all mind altering / psychoactive sample providers (Wales and wider UK) was 36 years and an average age of 31 years old (range: 14-68, the age range captured in 2013/14 was 14-61).

- Females - median age was 30 years and an average age of 29 years (range: 14-55 years).
- Males - median age was 36 years, with an average age of 31 years (range 14-68 years).

Chart 2: Profile of psychoactive sample providers



What ...

Most commonly identified substances

The most commonly identified chemical group of psychoactive substances were SCRAs. To date the WEDINOS project has profiled 32 SCRAs. Cocaine was the most commonly identified psychoactive substance. The most common legal/not currently controlled substance was the SCRA - 5F-PB-22. Chart 3 shows the most commonly profiled psychoactive substances from WEDINOS.

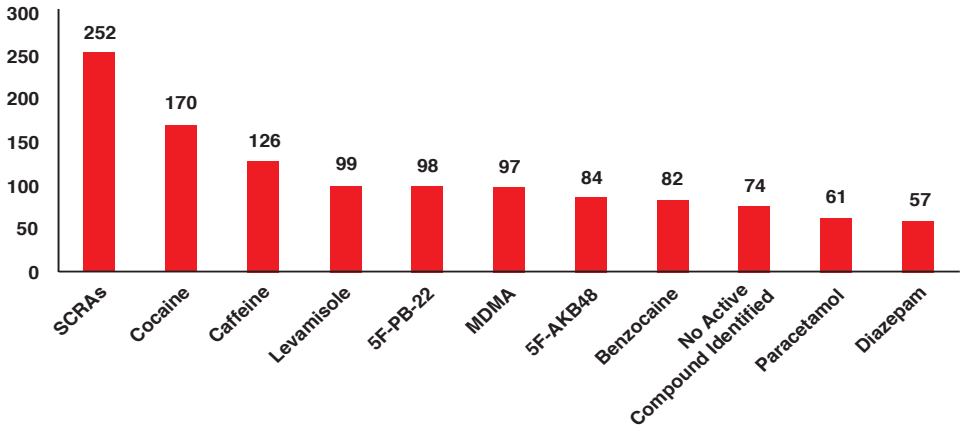
Levamisole was the most popular bulking/cutting agent identified, however it was found exclusively in samples that also contained cocaine. Of the 404 samples submitted to WEDINOS that were found to contain cocaine, 65 per cent (n=262) also contained levamisole.

Samples profiled as containing both cocaine and levamisole have also been found to contain, amongst other substances: methylhexamine, caffeine, mannitol, benzocaine, MDAI. Traditionally, levamisole has been seen purely as a bulking agent increasing the amount of product to enhance the profits of the seller. However, a recent in vivo study has indicated a synergism, with levamisole enhancing the effects of cocaine in stereotyped movements [iv.]. This potential benefit does need to be weighed against the risks as "potential complications associated with use of levamisole-laced cocaine include neutropenia, agranulocytosis, arthralgias, retiform purpura, and skin necrosis" [v.].

During the two years since project launch caffeine has consistently been found to be the most prevalent bulking/cutting agent. Consistent with previous findings it is a component in a diverse range of samples including substances from the stimulant, depressant and hallucinogenic drug categories.

Since the turn of 2015, an increasing number of samples have been profiled with caffeine found in isolation. During the quarter April to June 2015, it was decided to stop solely identifying caffeine as a bulking / cutting agent and begin to look at its use as a psychotropic substance within the stimulant category.

Chart 3: Most commonly identified mind altering/psychoactive substance WEDINOS samples.



iv. Tallarida CS et al. (2014). Levamisole and cocaine synergism: a prevalent adulterant enhances cocaine's action in vivo. Neuropharmacology; 79:pp.590-5. doi: 10.1016/j.neuropharm.2014.01.002.
v. Lee KC et al. (2012). Complications associated with use of levamisole-contaminated cocaine: an emerging public health challenge. Mayo Clin Proc 87(6):pp.581-6. doi: 10.1016/j.mayocp.2012.03.010.

Most commonly identified new psychoactive substances

The most commonly identified NPS groups are SCRAs and cathinones. Of the ten most commonly identified NPS profiled by WEDINOS in the last year, three are SCRAs and two are cathinones, as shown in Chart 4.

During the latter half of 2014 an increase in samples submitted and analysed that were found to contain either the tryptamine 5-MeO-DALT or the stimulant ethylphenidate was noted.

Of the NPS samples that were purchased as branded products, 46 per cent contained at least two substances, down from 80 per cent in 2013/14 and 11 per cent contained at least three down from 54 per cent. Four samples were found to contain four substances and one a total of five substances each.

Chart 4: Most commonly identified New Psychoactive Substances.

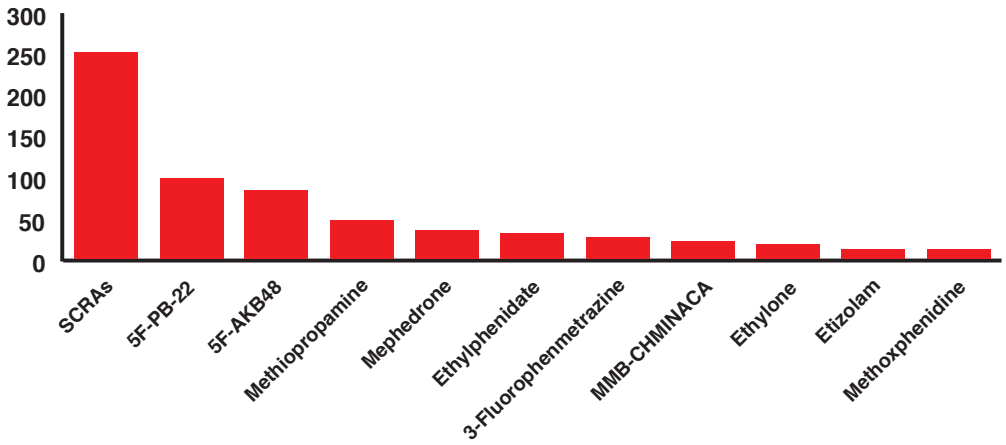


Chart 5: Top ten commonly identified New Psychoactive Substances

Position	2014/15	2013/14
1 Non-mover	5F-PB-22	5F-PB-22
2 Non-mover	5F-AKB48	5F-AKB48
3 Up one	Methiopropamine	Mephedrone
4 Down One	Mephedrone	Methiopropamine
5 Non-mover	Ethylphenidate	Ethylphenidate
6 Up two	3-Fluorophenmetrazine	5-MeO-DALT
7 New entry	MDMB-CHMICA	Ketamine
8 New entry	Ethylone	3-Fluorophenmetrazine
9 Non-mover	Etizolam	Etizolam
10 New entry	Methoxphenidine	Phenylethylamine

Changing laws, changing trends?

On 6th January 2015, the *Misuse of Drugs Act 1971* [vi.] was amended to include compounds captured by an extended definition of tryptamines to include 5-MeO-DALT as a Class A substance. Following, this ban 5-Meo-DALT has not been listed in the Jan-Mar 2015, Apr-Jun 2015 or the Oct 2014-Sept 2015 top ten most commonly identified substances; this despite being the sixth most commonly identified substance for the year Oct 2013-Sept 2014. Also, included in this change in legislation were:

- the synthetic opioid AH-7921
- the LSD-related compounds commonly known as ALD-52, AL-LAD, ETH-LAD, PRO-LAD and LSZ.

A similar trend in the reduction of samples following this change in legislation can also be seen in samples of blotter papers. Blotter papers are synonymous with the hallucinogenic substance LSD (lysergic acid diethylamide), however, in 2014 there was an increase in samples of blotter papers laced with LSD-related compounds (ALD-52, ETH-LAD, PRO-LAD, AL-LAD and LSZ); as these potent hallucinogens became available through some specialist websites. During this period 34 samples of blotter papers were submitted and 12 substances profiled. Since this legislative change, to date 12 samples of blotter papers have been submitted, with a far less diverse number of substances being profiled (four). The two most commonly identified substance being the currently legal / not controlled substance, 1P-LSD (five samples) and the Class A substance, LSD (four samples)

This trend in a reduction in the number of samples of a particular substance being submitted to WEDINOS following its legislative control is further evidenced by the 12 month Temporary Class Drugs Order (TCDO) implemented on the methylphenidate based substances and their derivatives on 27th June 2015. Since first being identified by WEDINOS in the quarter Jan-March 2014, ethylphenidate had been a mainstay in the WEDINOS top ten most commonly identified NPS substances moving from number 7 to number 3 (behind two SCRA's) in Apr-Jun 2015, being joined in the top ten by another of the five methylphenidate based substances profiled by WEDINOS Isopropylphenidate (a reporting form which was submitted to WEDINOS to the EMCDDA). Since the implementation of the aforementioned TCDO the number of samples containing methylphenidate based substances has fallen. From 27th June 2015 to 31st September 2015, three samples were profiled as containing ethylphenidate, two of which were purchased in the belief that they were cocaine, the third sample was purchased as ethylphenidate. No samples containing isopropylphenidate have been profiled during the same period. The pre-TDCO popularity of ethylphenidate was evidenced (Chart 4), where despite there only being three occasions where ethylphenidate was profiled, post-TCDO, it remains the fifth most commonly identified substance over the last year.

These trends in the reduction in submission of a substance following a legislative control measure may suggest that legislation has an effect on drug markets and choices. However, it appears that this is only the case in substances that were previously licit at the time of project launch (October 2013); as cocaine, MDMA and diazepam can be found in the top ten most identified substances (Chart 3) and mephedrone and ethylone are amongst the top ten NPS (Chart 5). It may therefore, be more indicative of the population using WEDINOS, with these individuals looking to consume psychoactive substances as safely as possible utilising a harm reduction provision such as WEDINOS, whilst also looking to remain within current legislation.

vi. Misuse of Drugs Act 1971. Chpt. 38. Available at: http://www.legislation.gov.uk/ukpga/1971/38 [Accessed 12th Dec 2015]

Legal status...

The following section relates to the 1,350 samples submitted to and analysed by the WEDINOS project between 1st October 2014 and 30th September 2015.

What has become increasingly evident is the cross over between the NPS drug market and the illicit drug market.

14 per cent of samples that were purchased / submitted in the belief that they were a controlled substance were, upon analysis, found to be non-controlled compounds; this is an increase from 8 per cent in 2013/14. For example three samples submitted as cannabis were found upon analysis to contain SCRAs. A sample submitted as methoxetamine contained methoxphenidine.

Likewise, overall 21 per cent of samples that were purchased / submitted in the belief that they were legal/not controlled, contained controlled substances, this is an increase from 18 per cent in 2013/14.

The increase in the number of substitutions of licit drugs with illicit drugs and vice versa begins to demonstrate a cross over between the two markets. As previously highlighted this raises concerns around unexpected psychological, physiological and social effects to the end user including potential criminal justice impacts.

As Chart 6 clearly indicates, many samples had a different legal classification to that believed by the purchaser.

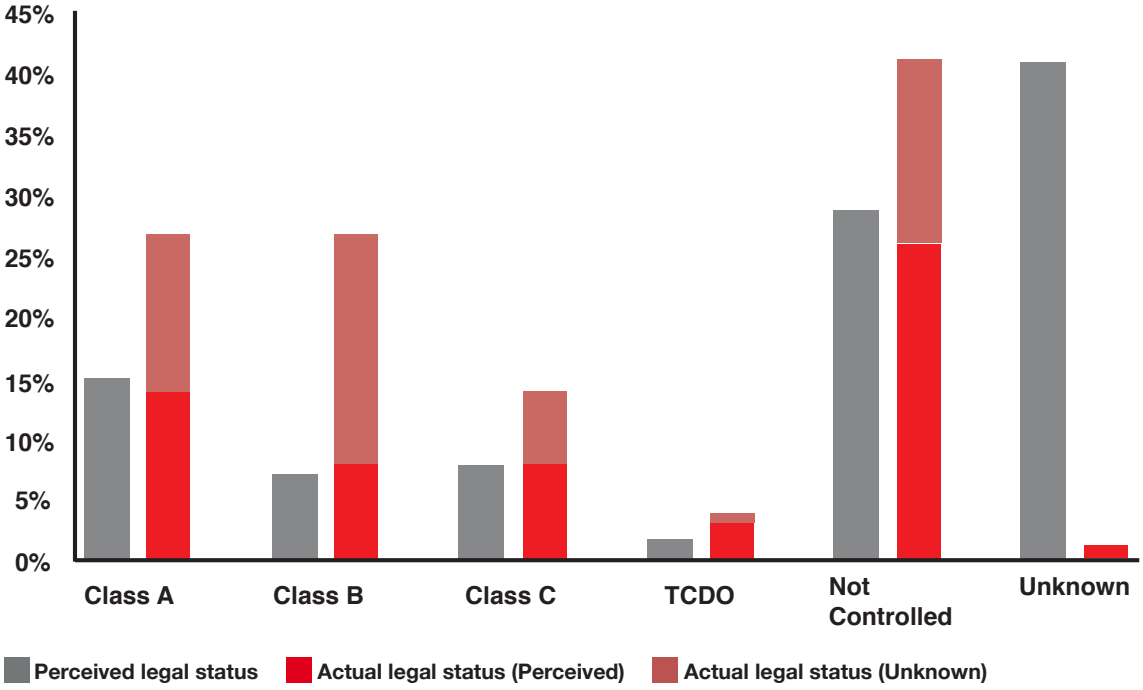
Excluding samples that were submitted with no information relating to their classification under the *Misuse of Drugs Act 1971* (n=551), samples changed classification from what the sample provider perceived, based on the intended purchase, to a different legal status following analysis.

In terms of numbers samples described as Class A decreased from 197 samples to 185. Class B rose from 93 to 112, as did Class C from 102 to 103. Samples described as legal fell from 385 to 353, whilst samples subject to a TCDO rose from 22 to 39. Nine samples could not be classified as there was an insufficient amount of material to analyse or were plant matter with no psychoactive properties.

Examples of these changes include:

Believed to be (purchase intent)	Found upon analysis to be
Cannabis	5F-PB-22 and 5F-AKB48
MDAI	MDMA
MDMA	alpha-PVP
MDMA	Ethylone
Methamphetamine	Ethylone
MDPV	25I-NBOMe and 25H-NBOMe
Amphetamine	Ethylphenidate
Legal product, branded ‘Ching’	Ethylphenidate
Legal product, branded ‘Banshee Dust’	Ethylone

Chart 6: Proportion of controlled and not controlled / legal – perceived and actual (Psychoactive Substances)

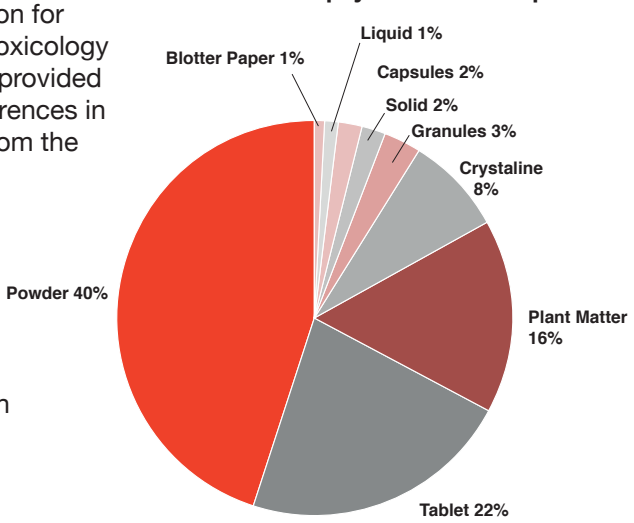


How ...

Form of sample

WEDINOS requests the 'form of sample' for each submission for two reasons; to ensure that the substance received in the toxicology laboratory matches to the description given by the sample provided (as part of chain of custody process); and, to note any differences in the forms of the same drug/compounds being submitted from the population including mechanisms for ingestion or use.

Chart 7: Form of psychoactive samples



Method of consumption

Assuming that all plant matter samples are smoked (unless stated otherwise, such as oral for Khat consumption or psychedelic mushrooms) and excluding samples where method of consumption was not described; samples (pills, liquids, tabs, granules etc) submitted to WEDINOS were ingested through a variety of methods.

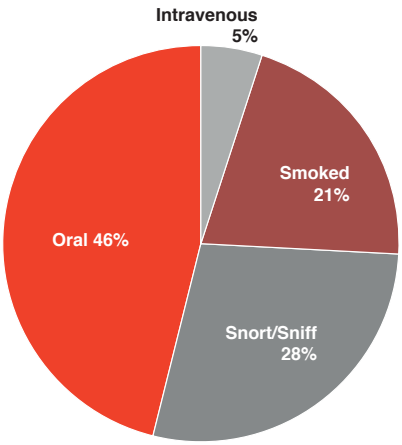
Consuming a substance orally (swallowing, bombing) was the most common method of consumption (46 per cent), followed by snort/sniff at 28 per cent, as shown in Chart 8. 21 per cent described smoking as the method of consumption, whilst 5 per cent stated intravenous administration, this up from 3 per cent in 2013-14. Injecting drug use carries with it inherent risks of bacterial and viral infection over and above the risks / toxicity of the substance being injected.

Substances submitted to WEDINOS that had intravenous listed as the method of consumption include:

- Amphetamine
- Ethylphenidate
- Heroin
- Mephedrone
- Methamphetamine

Injection of NPS, particularly mephedrone, has already been linked to clusters of hepatitis C infection amongst people who inject drugs in Wales. Concerns have also been highlighted amongst drugs services within Scotland as a result of individuals injecting ethylphenidate.

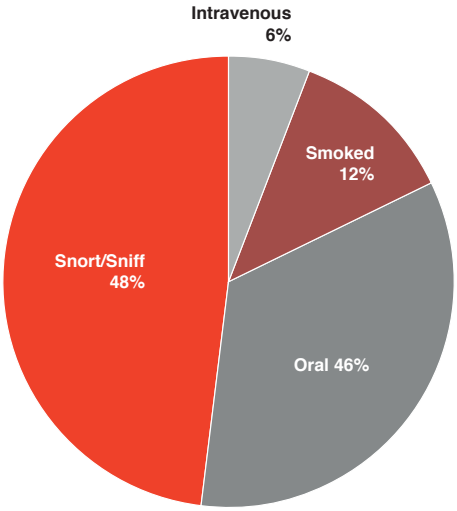
Chart 8: Method of consumption: All psychoactive samples



Focusing on the method of use for powders and crystalline materials, the most common method of consumption was snorting/sniffing with 48 per cent reporting this as shown in Chart 9. This represents almost a 20 per cent decrease from 59 per cent in 2013-14. Snorting/sniffing potentially caustic or toxic substances carries additional risks related to damage to the nasal passages as well as potential transmission of blood borne viral infection when sharing snorting paraphernalia in the precense of nasal passage damage and blood.
Of additional concern, is the 6 per cent reporting intravenous injecting of powders / crystalline materials, this is a slight increase from 5 per cent in 2013-14.
This coupled with the evidence from WEDINOS alongside other sources of substitution of one substance for another within the branded and non-branded NPS and illicit drug markets.

This is particularly concerning following samples that were found upon analysis to contain white heroin and the synthetic opioid, ocfentanil. Both of these substances are more potent than heroin. For more information on white heroin and ocfentanil, see the section Synthetic Opioids.

Chart 9: Method of Consumption: Powders



Synthetic Cannabinoid Receptor Agonists

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

The use of SCRAs has become more popular over the past few years. Following the first notification to the European Union EWS in 2008 (JWH-018 detected in Spice products), SCRAs now make up the largest chemical group monitored by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). In recent years, over 130 SCRAs have been detected by European early warning and drug testing systems.

As mentioned earlier, a total of 101 new substances were reported to the EU EWS in 2014 (up from 81 in 2013), continuing an upward trend in substances notified in a single year. As has been the case since 2011 notifications of cannabinoids have, along with synthetic cathinones, dominated the list of psychoactive substances notified to EWS. In 2014 SCRAs made up a third (n=30) of all notifications, in 2013 the figure was 36 per cent (n=29) of the 81 notifications.

Between project launch and September 2015 WEDINOS has profiled 32 SCRAs. Commonly these substances are profiled as a combination of SCRAs with up to six being profiled in a single product (Chronic Haze).

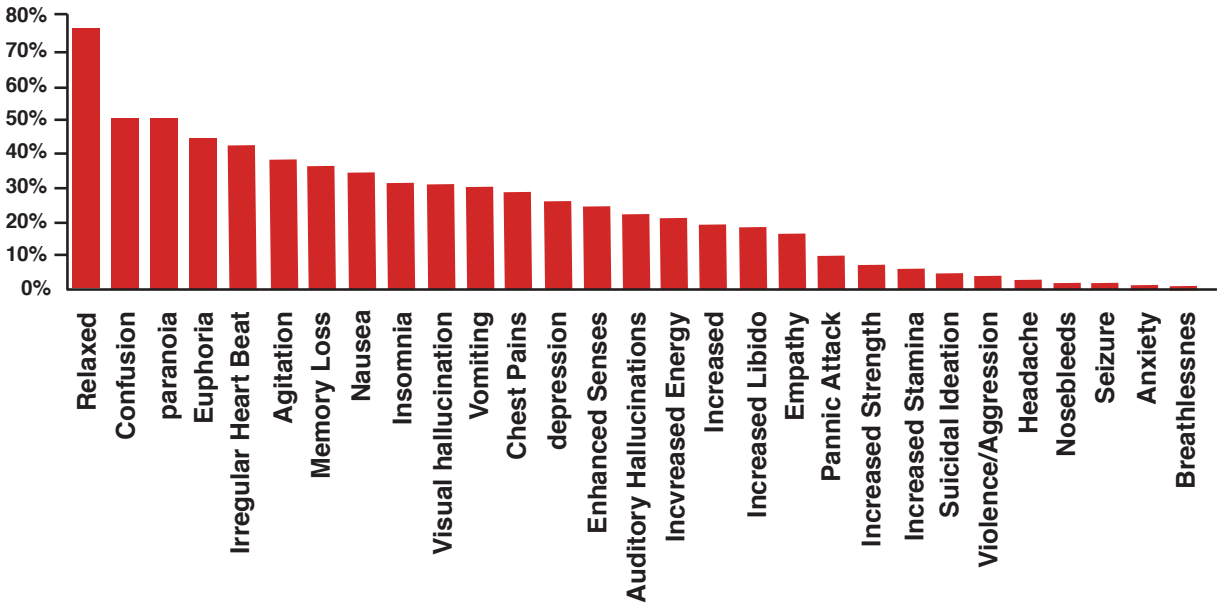
Most of the compounds identified by the WEDINOS project have been found in ready-to-smoke herbal products, this trend is also reflected in the United Nations Office on Drugs and Crime (UNODC) report: *Synthetic cannabinoids in herbal products*, although several samples have been in powder and tablet form and as liquids for use in an e-cigarette.

Although these substances have similar functions to Tetrahydrocannabinol (THC), producing some effects that are similar to THC they are not the same and are structurally different.

Most of the compounds identified by the WEDINOS project have been found in ready-to-smoke herbal products, this trend is also reflected in the UNODC report: Synthetic Cannabinoids in herbal products. Products of this type analysed to date have been found to have higher affinities for the CB1 receptor than THC and are full agonists of this site. THC in comparison acts as a partial agonist. WEDINOS has also identified SCRAs in powder and tablet form and as liquids for use in an e-cigarette.

Chart 10 shows the self-reported effects of samples submitted to WEDINOS by SCRA sample providers and the percentage of users who experienced each effect.

Chart 10: Reported Effects



From anecdotal reports, WEDINOS believes that the proportion of individuals experiencing seizures is higher than currently reflected. “Seizure” is not listed as an option for expected / unexpected effects on the WEDINOS sample and effects record at time of writing, and has only been reported within additional comments.

In 2015/16, WEDINOS will introduce seizures as an option on the downloadable sample and effects record [vii.] and advise services completing packs to endeavour to record seizures where they have been described as an effect of use by a sample provider.

Mella et al [viii.] believe that “seizures/status epilepticus may be the first recognized manifestation of synthetic cannabinoid toxicity” writing their piece *Neurology (April 6, 2015 vol. 84 no.14 Supplement P5.109)* with the objective of raising awareness of this issue amongst clinicians and the general population.

There are concerns around the potency of these substances with some SCRAs and blends appearing more potent than others. Coupled with this, WEDINOS has identified changes in the substance or combination of substances found some branded products. Examples: Clockwork Orange has been found to contain 5F-AKB48 in isolation, but also in combination with 5F-PB-22. The branded product Sweet Leaf Obliteration has been found to contain 5F-AKB48 and 5F-PB-22 in combination, but also MDMB-CHMICA in isolation. To July 2015, MDMB-CHMICA has been associated with a hospitalisation in Wales, 16 non-fatal intoxications across Germany (3), Austria (6) and Sweden (7) and six deaths – two in Germany and four in Sweden.

The SCRAs most commonly identified by the WEDINOS project are 5F-PB-22 and 5F-AKB48. Currently neither of these substances are controlled by the *Misuse of Drugs Act 1971*, nor do they fall under the controls of the Medicines and Healthcare products Regulatory Agency or the *Medicines Act 1968*.

The Global Drugs Survey findings for 2015 [ix.] found that the risk of SCRA users seeking emergency medical treatment (EMT) was 30 times higher than those who had used herbal cannabis. From integration of the Global Drugs Survey data Winstock et al found that not only was the relative risk of seeking EMT greater amongst SCRA users, but also that they presented with significantly more symptoms than those attending with cannabis related concerns [x.].

Psychosis has also been reported amongst frequent SCRA users. Presentations were characterised by paranoid delusions, ideas of reference and a disorganised, confused mental state [xi.]. Most patients presenting with psychosis reported feelings of depression and 40% suicidal ideation. Although psychotic symptoms did diminish in most case, 30% of patients were still suffering psychotic episodes 8-months later [xii.].

vii. Public Health Wales. WEDINOS Project Sample and Effects Record. 2014.
Available at: http://www.wedinos.org/resources/downloads/WEDINOS_Sample_and_Effect_Record_web.pdf [Accessed 8th Dec 2015]

viii. Mella D et al. (2015). Cannabinomimetic neurotoxicity. Neurology; 84 (14) Supplement P5.109.
Available at: http://www.neurology.org/content/84/14_Supplement/P5.109 [Accessed 15th Dec 2015]

ix. Global Drugs Survey. (2015). The Global Drug Survey 2015 findings.
Available at: http://www.globaldrugsurvey.com/the-global-drug-survey-2015-findings/ [Accessed 8th Dec 2015]

x. Winstock A et al. 2015. Risk of emergency medical treatment following consumption of cannabis or synthetic cannabinoids in a large global sample. J Psychopharmacol 29(6):pp.698-703. doi: 10.1177/0269881115574493.

xi. 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 12th Dec 2015]

xii. Hurst D, Loeffler G, McLay R. (2011). Synthetic cannabinoid agonist induced psychosis a case series. APA poster. San Diego: Naval Medical Centre.
Available at: http://www.med.navy.mil/SiteCollectionDocuments/SPICE/Spice%20APA%20poster.pdf [Accessed 12th Dec 2015]

Van Amsterdam, Brunt and Van den Brink [xiii.] from their paper review of SCRAs, with a particular focus on psychosis inducing risk, found that 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 cannabidiol (CBD) within SCRA products. Although there are few reviews around risks related to SCRAs, and the comparative risks between SCRAs and cannabis there are an increasing number of case reports in relation to harms linked to the use of SCRAs. One such harm is acute kidney injury as a result of the use of SCRAs [xiv. - xvi.].

Routes of administration for these substances reported to WEDINOS include smoking, vaporising, snorting and oral consumption.

Opioids

Heroin is the most common opioid on the European drug market. Heroin is produced by the conversion of opium tapped from the seed head of the annual flowering plant, the opium poppy (Papaver somniferum). Within the tapped opium there are over 40 different alkaloids; these include morphine, codeine, noscapine and papervirine.

In the purification process of opium for conversion to heroin these alkaloids should be removed. However, within street heroin some of these alkaloids are often not removed, remaining as impurities of origin.

Most street heroin is brown in colour, and what is known as base heroin, often containing impurities of origin as well as other bulking / cutting agents such as; paracetamol, Mannitol, caffeine and fluoxetine (WEDINOS sample analysis) although white heroin is also available.

White heroin is the result of the purification of heroin base to heroin hydrochloride (a fine white powder). This extra process turns it into a salt form, making it very pure and water soluble; unlike brown heroin that requires the addition of some kind of acid (usually citric acid or ascorbic acid (Vit C)) to make it soluble in water. However, it should be noted that while the expectation is for white heroin to be more potent and pure than its brown base form, this cannot be guaranteed as the white powder may be adulterated with bulking and cutting agents that are also white powders.

The Office for National Statistics report, *Deaths related to drug poisoning in England and Wales*, 2014 showed that the number of deaths involving heroin and/or morphine increased by almost two thirds between 2012 and 2014 from 579 to 952.

The number of deaths from drug misuse in Wales have decreased by 16 per cent on the previous year, with a total of 113 deaths. This continues a downward trend observed over the last five years, and since 2008 deaths from drug misuse have decreased by 30 per cent.

xiii. 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.
xiv. Thornton SL et al. (2013). Synthetic cannabinoid use associated with acute kidney injury. Clin Toxicol 51(3): pp.189-90
xv. Buser GL et al. (2014). Acute kidney injury associated with smoking synthetic cannabinoid. Clin Toxicol 52(7): pp.664-73
xvi. Srisung W et al. (2015). Synthetic cannabinoids and acute kidney injury. Proc (Bayl Univ Med Cent); 28 (4); pp. 475-77. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4569229/pdf/bumc0028-0475.pdf [Accessed 8th Dec 2015]

Much work has been undertaken to develop effective and cost-effective interventions to reduce drugs overdoses and deaths across Wales over the last decade which, through a harm reduction approach, encourages those who are using drugs to come forward for help.

These interventions include the provision of take-home Naloxone, an opiate antagonist used in the event of opiate overdoses [xvii].

The Public Health Wales annual profile for substance misuse 2014-15 [xviii] shows that opioids account for a considerably more admissions to hospital than any other substance for individuals within the 25-49 age group, 1,338 admissions; this figure accounts for 46 per cent of hospital admissions for poisoning with a named illicit drug for this age group.

In 2013, law enforcement agencies across Europe seized other opioids including opium and the medicinal products morphine, methadone, buprenorphine, fentanyl and tramadol.

Synthetic Opioids

Synthetic opioids are man-made substances that have been manufactured to mimic the effects of natural opioids including opium. This category of substances includes prescription only medicines (POMs) including fentanyl and pethidine (fentanyl and pethidine are also controlled by the *Misuse of Drugs Act 1971* as a Class A substance), and NPS including AH-7291 and MT-45 which have very little history of use and no evidenced medicinal uses.

14 new synthetic opioids have been reported to the EU EWS since 2005, among which are several highly potent uncontrolled fentanyls [xix].

According to the *Fentanyl in Europe – EMCDDA trendspotters study*, the emergence of synthetic opioid use, and more explicitly fentanyls within the European drug market dates back to the mid-1990s.

Although, the use of fentanyls has been reported across Europe, use predominates in Eastern European countries where a substantial rise in fentanyl use is seen during periods where heroin has been in short supply e.g. Bulgaria (2010/11) and Slovakia (2011). In 2012, there was evidence of localised fentanyl use and fentanyl-related deaths amongst opioid users in Sweden, Finland and Germany. In Estonia, fentanyl use has been described as endemic in the injecting drug use population, with fentanyls becoming the most used opioid since 2000.

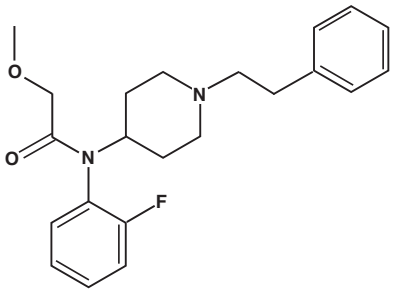
xvii. Public Health Wales.2015. Harm Reduction Database Wales: Take Home Naloxone 2014-15. Substance Misuse Programme, Health Protection Division. Available at: http://www2.nphs.wales.nhs.uk:8080/SubstanceMisuseDocs.nsf/85c50756737f79ac80256f2700534ea3/1d876d9a88e4bab080257eb5003ad902/$FILE/HRD%20Wales%20-%20Take%20Home%20Naloxone%202014-15%20FINAL.pdf [Accessed 14th Dec 2015]

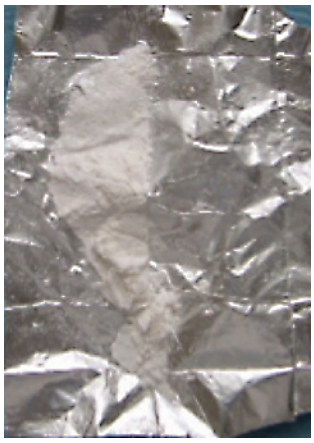
xviii. Public Health Wales. 2015. Reading between the lines: The annual profile for substance misuse 2014-15. Substance Misuse Programme, Health Protection Division. Available at: http://www2.nphs.wales.nhs.uk:8080/SubstanceMisuseDocs.nsf/5633c1d141208e8880256f2a004937d1/9033e325d64e85980257eed0031a86a/$FILE/Reading_between_the_lines_Annual_Profile_Substance_Misuse_Wales_2014-15.pdf [Accessed 14th Dec 2015]

xix. European Monitoring Centre for Drugs and Drugs Addiction. 2015. European drug report 2015: Trends and developments. Lisbon, EMCDDA. Available at: http://www.emcdda.europa.eu/attachements.cfm/att_239505_EN_TDAT15001ENN.pdf [Accessed 14th Dec 2015]

Ocfentanil

Ocfentanil is a potent synthetic opioid substance structurally related to fentanyl. **Ocfentanil is a naloxone-reversible substance.**





Ocfentanil is an opioid analgesic. It is an analogue of fentanyl that was developed in the early 1990s. It is similar to fentanyl in effects, producing strong analgesia and sedation, but is slightly more potent. Side effects of fentanyl analogues are similar to those of fentanyl, and include itching, nausea and potentially serious respiratory depression which can be life-threatening.

More potent than heroin, it has similar effects to fentanyl producing strong analgesia and sedation. However, it is slightly more potent than fentanyl, with 3µg/kg of ocfentanil being equivalent to 5µg/kg of fentanyl [xx], and as such is a clear risk for overdose.

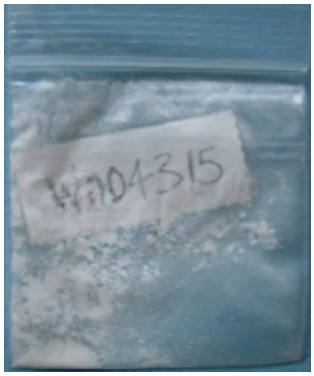
Between 19th March 2015 and 16th July 2015, WEDINOS received six samples in powder form that upon analysis were found to be ocfentanil. Of these powders, three were white powders and three brown powders. The route of administration for these samples was snort/sniff in two cases, smoked in one and the remaining three samples did not have any details around the route of administration. Effects experienced included: euphoria, relaxation, nausea, chest pains, paranoia and agitation.

Following analysis of these samples, the following substances were identified in varying combinations. Three combinations were profiled:

- Ocfentanil, paracetamol and caffeine
- Ocfentanil, paracetamol, caffeine and mannitol
- Ocfentanil, paracetamol, caffeine and methamphetamine.

xx. Fletcher JE et al. (1991). Comparison of ocfentanil and fentanyl as supplements to general anesthesia. Anesth Analg 73(5):pp.622-6.

Acetyl Fentanyl



WEDINOS sample W004315 was submitted in the belief that it was the benzodiazepine analogue Etizolam; upon analysis this sample was found to contain acetyl fentanyl in isolation. Effects listed by the sample provider were: relaxation, nausea and vomiting.

Acetyl fentanyl is a potent synthetic opioid analgesic and is derivative of fentanyl.

It is suggested that acetyl fentanyl is 5 to 15 times more potent than heroin [xxi].

It is thought that naloxone will have the same reversal effect for acetyl fentanyl as it does for fentanyl and other synthetic opioids, however due to its higher potency compared to heroin it may require a larger dose [xxii].

Acetyl fentanyl effects are reported to include euphoria, altered mood, drowsiness, constriction of the pupils, cough suppression, constipation and respiratory depression.

Commonly reported routes of administration of acetyl fentanyl include intravenous injection, snorting and smoking.

xxi. Higashikawa Y and Suzuki S. (2008). Studies on 1-(2-phenethyl)-4-(Npropionylanilino) piperidine (fentanyl) and its related compounds: structure-analgesic activity relationship for fentanyl, methyl-substituted fentanyls and other analogues. Forensic Toxicol 26:pp.1-5.
xxii. Roberts JR. (2013). Acetyl fentanyl: new drug of abuse more common than assumed. Emerg Med News 35:1-28.

3,4-methylenedioxy-N-methylamphetamine (MDMA)

Following on from our focus on MDMA in the WEDINOS 2013/14 annual report; and hearing analytical reports of high dose MDMA pills from across Europe and anecdotal reports of increased potency and popularity of MDMA powders and crystalline materials WEDINOS looks at samples submitted for analysis in 2014/15 that were purchased in the belief that they were MDMA.

MDMA is a psychoactive substance chemically related to amphetamines. It acts as both a stimulant and psychedelic. MDMA mainly affects brain cells that use the chemical serotonin to communicate with each other. Serotonin helps to regulate mood, aggression, sexual activity, sleep, and sensitivity to pain.

First synthesised and patented by Merck pharmaceutical company in 1912 and 1914 [xxiii.] respectively; MDMA was originally developed by Merck who looked to develop a vasoconstrictor to help reduce bleeding. The exact timeline for MDMA becoming a recreational drug is unclear; however the drug gained prominence in late 1970s.

EMCDDA *European drug report – Trends and developments 2015*, estimates 0.6 per cent of European adults (2.1million) aged 15-64 had used MDMA in the last year, with 3.6 per cent (12.3million) having used in their lifetime. Ecstasy usually refers to the synthetic substance MDMA.

According to the UK Focal Point report 2014, MDMA powder continues "to be widespread and in demand across the UK", with consumers generally being from younger age groups. Although there was no data for pill strength/dosage in the UK Focal Point report 2014 for 2013, previous reports have shown increases in MDMA content. MDMA content rose 31mgs between 2011 and 2012 to 102mg, which was an increase of 54mgs since 2006 in 2014/15 we have also seen analytical reports from Europe where Ecstasy pills have been found to contain over 300mgs of MDMA.

The Global drugs survey 2015 [xxiv.] has seen a year on year increase in the number individuals who used MDMA in the last year attending Emergency Departments for treatment as a result of their use from 0.3 per cent in 2013 to 0.6 per cent in 2014 rising to 0.9 in 2015

The above coupled with the risk of contamination of MDMA or its substitution with other substances, increases the concern for the welfare of individuals using, due to variants in potency and time of onset. In 2013/14 WEDINOS 36 per cent (n=11) of these samples submitted as MDMA/ Ecstasy did not contain MDMA, but other psychoactive substances including: BZP, MeOPP, Methylone, Cocaine, 6-MAPB, alpha-PVP and Finasteride.

Between 1st October 2014 and 30th September 2015 WEDINOS analysed 76 samples that were submitted as e, ecstasy and MDMA.

The samples were submitted in the following forms: 55 per cent tablet (n=42), 25 per cent crystalline (n=19), 12 per cent powder (n=9), 5 per cent granules (n=4), 3 per cent capsules (n=2).

xxiii. MDMA.net. (2014). E. Merck's 1914 MDMA patent. (online). Available at: http://www.mdma.net/merck/mdma-patent1.html [Accessed 8th December 2015]
xxiv. Global Drugs Survey. (2015). The Global Drug Survey 2015 findings.
Available at: http://www.globaldrugsurvey.com/the-global-drug-survey-2015-findings/ [Accessed 8th Dec 2015]

Of these samples 52 per cent (n=39) contained MDMA only, 46 per cent (n=35) contained another substance(s), 1 per cent (n=1) MDMA and another substance and 1 per cent (n=1) an unknown compound (not enough material to conduct further analysis).

The most commonly identified MDMA substitutes were the synthetic cathinones: alpha-PVP, methylone and ethylone.

Other substances identified include: other synthetic cathinones, piperazines, synthetic cannabinoid receptor agonists and image and performance enhancing drugs.
Effects reported by sample providers who believed they had purchased MDMA; that upon analysis were found to contain different compounds, include:

Agitation
Anxiety
Auditory hallucinations
Breathlessness
Chest pains
Confusion
Depression
Empathy
Enhanced senses
Euphoria
Increased confidence
Increased energy
Increased libido
Increased stamina
Insomnia
Irregular heartbeat
Nausea
No effect
Panic attack
Paranoia
Relaxed
Visual hallucination
Vomiting

The law is changing

(expected April 2016)

The Psychoactive Substances Bill

The UK government has proposed a UK wide general ban on psychoactive substances.

Psychoactive substance:
"a substance capable of producing a psychoactive effect in a person who consumes it".

A substance produces a psychoactive effect in a person "if, by stimulating or depressing the person's central nervous system, it affects the person's mental functioning or emotional state".

- Possession of a psychoactive substance **will not be an offence**, (except in a 'custodial institution')
- It **will be an offence** to produce, supply, offer to supply, possess with intent to supply, import or export psychoactive substances
- Nicotine, alcohol, caffeine and medicinal products (as defined by the Human Medicines Regulations (2012)) **will be exempt**
- **WEDINOS** does not fall within the scope of the Psychoactive Substances Bill, as such; **no offence would be committed** by those participating in the programme.

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