



# **Nitazenes and Contamination of Heroin**

## **issues and responses**

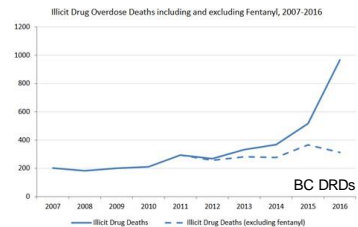
As these new substances have a rapidly evolving evidence base, this briefing will be revised as new intel emerges. The most up to date version can be found on the Safer Cornwall website.

**Revised May 2024**

## An Inter-Continental Starting Point



- American opioid crisis intersection of following key issues:  
Overprescribing of Oxycontin leading to significant dependency  
FDA restrictions on Oxy pushed people towards street drug market
- initially imported fentanyl saturated market and then Mexican cartels start to manufacture own fentanyls from imported precursors
- Restrictions in access to harm reduction measures and drug treatment on a state by state basis affected level of



fatalities

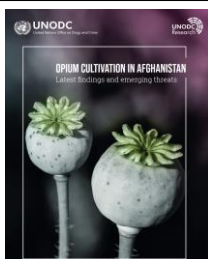
- Our starting point is different:
  - not the same high level of prescribed opioid dependency
  - 95% of our street heroin was Afghani brown heroin
  - the fentanyls did start to appear on the UK market – sometimes sold as “china white” or appearing as a cut in heroin – but not at a significant level.
  - so we hadn’t seen the same level of fatalities in the UK drugs market...



	2022	2021	2020	2019	2018	2017	2016	2015	2014	2013	2012	2011	2010
Fentanyl	57	58	57	59	74	75	58	34	40	22	22	31	10
Fentanyl analogues	0	3	2	1	31	31	1	1	0	0	2	0	0

## Heroin shortage

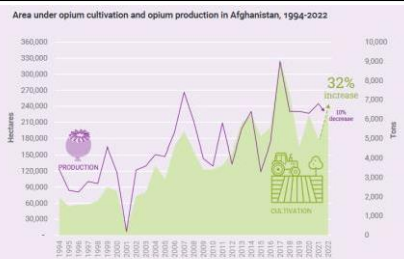
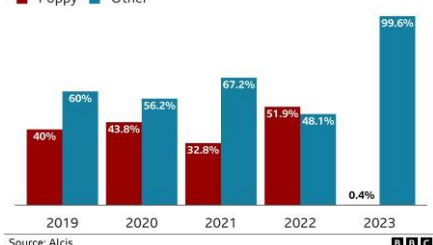
**KFX**  
Leading of Substance



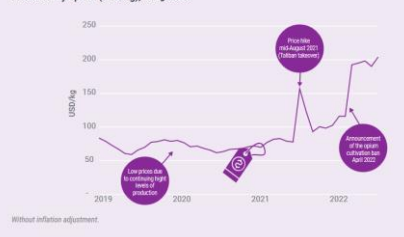
### How poppy cultivation in Helmand has fallen

Percentage of agricultural land area by crop

■ Poppy ■ Other



### Prices of dry opium (USD/kg), 2019-2022



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## What happens as heroin purity drops?

**KFX**

The emergence of novel opioids hasn't in the past in the UK been enough to create a tilt away from "traditional" heroin markets.

But the combination of reduced production and increased cost of brown heroin in Afghanistan PLUS Brexit impeded smuggling routes PLUS high potency/low weight synthetics could represent a tipping point.

Increased production in Asia (e.g. Myanmar won't significantly impact the UK market in short term so production drop in Afghanistan likely to have a sustained impact in UK.

### Increased risk of OD

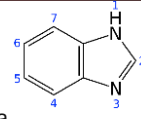
- **Increased importation of synthetic opioids to fill gap**
  - increase in nitazenes
- **Increased adulteration – cut with benzos, xylazine**
- **Drop in purity of heroin in UK - already observed**
  - some areas there is no diamorphine in the "heroin."
- **Increased polydrug use**
- **Shift from smoking to injecting – some reports that "brown" isn't smoking well**
- **more injecting complications - observed**
- **Switch to other substances – Spice, "Dust" - noted in some areas**
- **(catalyst for accessing treatment)**

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## Nitazenes

KFX

"Nitazenes" are a family of drugs called **benzimidazole opioids**  
 They are derived from **benzimidazole**  
**1950s** – developed by CIBA but never taken to market  
**2019 Isonitazene** in drugs and post OD toxicology in Europe and North America



The ACMD report on Nitazenes says:

*"The benzimidazole ring structure is, however, also found in a wide range of human and animal medicines..."*

*The 2-Benzyl benzimidazoles are synthetic opioids and can be prepared in only a few steps from readily available, uncontrolled precursors."*

This makes the family of drugs much harder to regulate as the core structure and precursors are harder to control.

In the UK the benzimidazole opioids already identified and possible likely analogues were brought under the Misuse of Drugs Act in April 2024.

### N-desethyl Isonitazene

"...a study in rats found...N-desethyl isotonitazene provided pain relief at a dose nearly ten times smaller than that needed for fentanyl, and around 1,400 times less than that for morphine, to see the same effect. N-desethyl isotonitazene causes apnea (where breathing stops) at about a third of the dose of fentanyl. It also takes much longer to recover normal breathing after N-desethyl isotonitazene (208 minutes) compared with fentanyl (67 minutes). One must assume, therefore, that some nitazenes may have the potential to be more deadly than fentanyl and heroin."

<https://theconversation.com/nitazenes-synthetic-opioids-more-deadly-than-fentanyl-are-starting-to-turn-up-in-overdose-cases-212589>

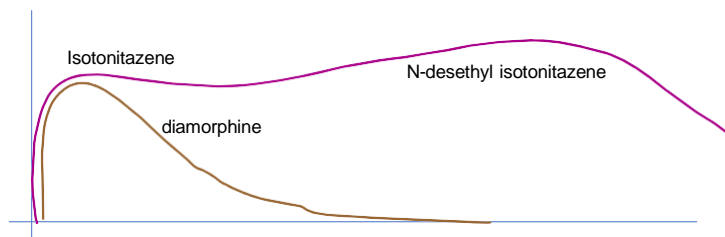
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## Longer duration and increasing potency

Isonitazene produces a long acting metabolite **N-desethyl isotonitazene** which is in highly potent (possibly more so than the parent drug) and so overdoses may not be rapid – and the period which a casualty may be unwell is longer than for other drugs.  
 meaning the Overdose risk window is far longer...  
 but we are not entirely clear how long.

### Implications:

- may be thought to be OK in the initial lower intoxication phase
- supervise for longer after OD revival
- Significantly higher risk of re-overdosing much later  
 longer window for overdose risk in hostels/custody/peer education settings



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## Relative potency of key opioid agonists



Drug	AKA	Potency (x morphine)	Law
Codeine		1/10	CD: PM/POM (depends on strength)
Tramadol		1/10	CD:POM
Dihydrocodeine	(DF118)	1/5	CD: PM/POM (depends on strength)
Pethidine		1/3	CD:POM
Morphine (oral)	MST, Oramorph	1	CD: PM/POM (depends on strength)
Flunitazene		1	
Oxycodone	Oxycontin	1.5-2	CD:POM
Morphine (IV)		3	CD:POM
Methadone	Physeptone	3-4	CD:POM
Diamorphine	Heroin	4-5	CD:POM
Hydromorphone	Palladone	5	CD:POM
Desomorphine	"Krokodil" Permonid	8	CD
Oxymorphone		7	CD/POM
Acetyl fentanyl		15	CD
Buprenorphine	Subutex, Temgesic	40	CD:POM
Etazine		70	CD
Protonitazene		130	
Isonitazene		500	CD
Fentanyl	Duragesic	50-100	CD:POM
Etonitazepipne		100	CD
Metonitazene		1000	CD
N- Desethyletonitazene		1000	CD
Etonitazene (N-pyrrolidino etonitazene) "Pyro"		1000	CD
(Etorphine) Wildenil		1000-3000	CD/POM
3-methyl fentanyl		6000	CD
(Carfentanyl)		10,000-100,000	CD/POM

[https://en.wikipedia.org/wiki/List\\_of\\_benzimidazole\\_opioids](https://en.wikipedia.org/wiki/List_of_benzimidazole_opioids)

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## Relative Potency



Street diamorphine at 20% purity

£10 bag = 100mg      20% purity= 20mg



Isonitazene is 500 x oral morphine so 100x IV diamorphine

20mg (20,000mcg) diamorphine IV = 200mcg IV isonitazene (0.2mg)

A poppy seed weighs 300mcg



So the equivalent dose of £10 brown heroin at 20% pure would be a little less than the size of a poppy seed if it were pure isonitazene.

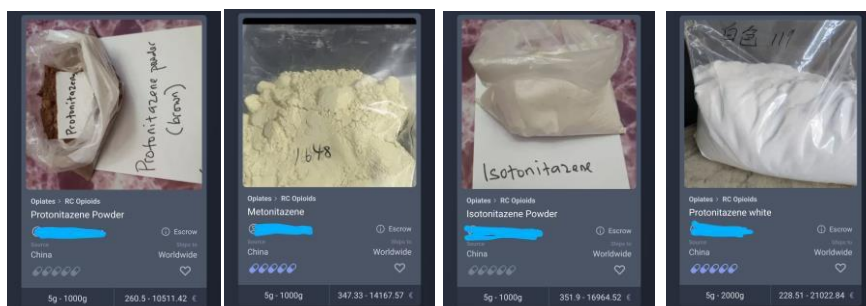
Imported diamorphine at 80% - 1kg = 800g diamorphine

Same quantity in terms of Isonitazene: 8g of Isonitazene

Same quantity in terms of Etonitazene: 4g of Etonitazene

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## Supply cost profit



### A crisis for prisons?

1g isonitazene = 500g morphine  
 = 100g pure heroin  
 = 500g of "street heroin" at 20%

In prison 1g smuggled in would need to be diluted with 0.5kg of bulking agent to make it lower risk. Without scales and without a mixer. Which leaves dangerous hotspots.

10g costs £600  
 10g = 1kg pure diamorphine (1000g)  
 1000g = 5kg "brown" @ 20% purity  
 5000g = 50,000 £10 bags  
 £500,000

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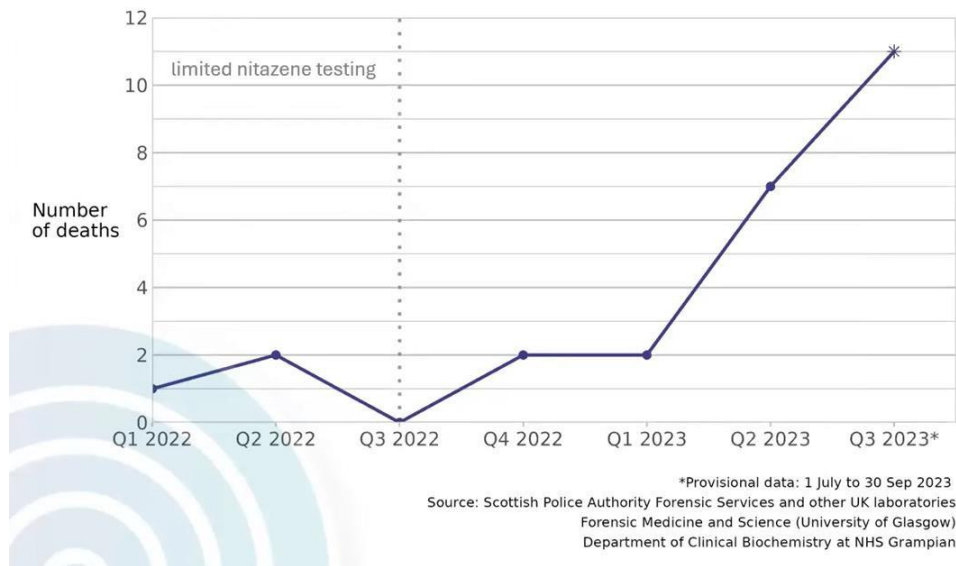
## Known Fatalities



- 24 deaths attributed to Isonitazene in 2021 [acmd]
- ONS reports 39 "Novel Opiate" drug related deaths in 2022
- NCA cites "54 deaths in six months to December 2023" and a possible implication in 40 other cases under investigation
- Clusters of fatalities in UK and Ireland; e.g. 16 reported in Birmingham
- Unclear number of non-fatal overdoses
- Some fatalities and non-fatal overdoses may have been incorrectly attributed to fentanyl

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## Recent Scottish ODs



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<p><b>W039044</b></p> <p>Date Received: 26 Sep 2023</p> <p>Postcode: E11 -</p> <p>Purchase Intent: Oxy</p> <p>Package Label: Oxy</p> <p>Sample Colour: Green</p> <p>Sample Form: Tablet</p> <p>Consumption Method: Not Stated</p> <p>Self-Reported Effects: Not Stated</p> <p>Sample Upon Analysis (Major): Metonitazene</p> <p>Sample Upon Analysis (Minor):</p>	<p><a href="#">Click to Enlarge</a></p>
<p><b>W038828</b></p> <p>Date Received: 15 Sep 2023</p> <p>Postcode: SE15 -</p> <p>Purchase Intent: Oxycodone</p> <p>Package Label: Not Stated</p> <p>Sample Colour: Yellow</p> <p>Sample Form: Tablet</p> <p>Consumption Method: Not Stated</p> <p>Self-Reported Effects: Not Stated</p> <p>Sample Upon Analysis (Major): Metonitazene</p> <p>Sample Upon Analysis (Minor):</p>	<p><a href="#">Click to Enlarge</a></p>
<p><b>W038944</b></p> <p>Date Received: 22 Sep 2023</p> <p>Postcode: CF37 -</p> <p>Purchase Intent: Diazepam</p> <p>Package Label: Diazepam</p> <p>Sample Colour: White</p> <p>Sample Form: Tablet</p> <p>Consumption Method: Oral</p> <p>Self-Reported Effects: No Effect</p> <p>Sample Upon Analysis (Major): Bromazolam, Metonitazene</p> <p>Sample Upon Analysis (Minor):</p>	<p><a href="#">Click to Enlarge</a></p>
<p><b>W038725</b></p> <p>Date Received: 11 Sep 2023</p> <p>Postcode: G83 -</p> <p>Purchase Intent: Diazepam</p> <p>Package Label: Benzodien</p> <p>Sample Colour: White</p> <p>Sample Form: Tablet</p> <p>Consumption Method: Not Stated</p> <p>Self-Reported Effects: Not Stated</p> <p>Sample Upon Analysis (Major): Bromazolam, Metonitazene</p> <p>Sample Upon Analysis (Minor):</p>	<p><a href="#">Click to Enlarge</a></p>
<p><b>W038950</b></p> <p>Date Received: 22 Sep 2023</p> <p>Postcode: WF10 -</p> <p>Purchase Intent: Diazepam</p> <p>Package Label: Diazepam</p> <p>Sample Colour: Blue</p> <p>Sample Form: Tablet</p> <p>Consumption Method: Oral</p> <p>Self-Reported Effects: Increased Confidence, Increased Stamina, Relaxed, Chest Pains, Irregular Heartbeat, Paranoia, Memory Loss, Confusion, Panic Attack, Agitation, Violence/Aggression, Insomnia, Depression, Sweating</p> <p>Sample Upon Analysis (Major): Bromazolam, Metonitazene</p> <p>Sample Upon Analysis (Minor):</p>	<p><a href="#">Click to Enlarge</a></p>
<p><b>W038754</b></p> <p>Date Received: 13 Sep 2023</p> <p>Postcode: SW16 -</p> <p>Purchase Intent: Heroin</p> <p>Package Label: Not Stated</p> <p>Sample Colour: Brown</p> <p>Sample Form: Powder</p> <p>Consumption Method: Smoked</p> <p>Self-Reported Effects: Breathlessness, Paranoia, Memory Loss, Confusion, Loss of consciousness, Agitation, Violence/Aggression, Insomnia</p> <p>Sample Upon Analysis (Major): Paracetamol, Isotonitazene, Caffeine, Heroin, Nicotine</p> <p>Sample Upon Analysis (Minor):</p>	<p><a href="#">Click to Enlarge</a></p>
<p><b>W038755</b></p> <p>Date Received: 13 Sep 2023</p> <p>Postcode: SW16 -</p> <p>Purchase Intent: Heroin</p> <p>Package Label: Not Stated</p> <p>Sample Colour: Brown</p> <p>Sample Form: Powder</p> <p>Consumption Method: Smoked</p> <p>Self-Reported Effects: Breathlessness, Paranoia, Memory Loss, Confusion, Loss of consciousness, Agitation, Violence/Aggression, Insomnia</p> <p>Sample Upon Analysis (Major): Paracetamol, Caffeine</p> <p>Sample Upon Analysis (Minor): Isotonitazene, Nicotine</p>	<p><a href="#">Click to Enlarge</a></p>

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## Key HR messages



- **Ideally use with company...**
  - or a place you will be found
  - or using a “buddy app” if no alternative
- **Ensure Naloxone and a phone is to hand**
- Always call an ambulance and use naloxone if opioid OD suspected
- Don't use depressant drugs in combination if possible but be aware it may be pre-mixed in what you bought;
- Sample or use low dose from new batches
- Change route if you can – smoke instead. There is still a significant risk of fatal overdose with smoking and snorting but it may reduce risk to a degree.
- Be aware of hot-spots
  - mixes of coarse and fine powders will never be even; a bag won't have an even mix in it so will vary in strength
- Don't use at the same time in groups
  - ideally have a sober sitter
- Share negative experience or unusual experiences with pe
- (use test strips – **won't detect all analogues**)
- (send samples to Wedinos)



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## Taking care with messages



- Avoid possibly promotional terms like “high strength” “strong” or “potent”
- *“Warning: potent batch of heroin found in...”* promotional
- *“Warning dangerous contaminant in local heroin may have caused recent deaths and hospitalisation”* – stresses risk
- Focus on
  - risk (wounds, OD, fatalities)
  - harm reduction (don't use alone, naloxone, treatment)
  - local relevance and timeframe
    - too many notices will lose impact; keep them local
    - keep them up as long as needed
    - speak to people don't just put posters up
    - discuss in groups
- You don't need to specify the drugs found – if you do ensure it's evidenced by toxicology and not hearsay
- Too much detail can give a false sense of security
  - e.g *“light tan coloured heroin runs orange on foil...”* – can make people think their own batch of drugs is safe
- When circulating emails in house always link back to the source: where did this message come from? How reliable is it? How old is it?

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## Targeting Non-Opiate Users



- At present the targeting of messages and Naloxone is at opiate users. However we are seeing significant increase in nitazenes as a cut in street-benzos.
- Isonitazene orally is estimated at 10x potency of oral morphine (2x potency of IV diamorphine) so in itself represents a risk of OD.

In combination with benzodiazepines the risk of fatal OD is elevated.

- While people using street benzos already in contact with drug services will be aware of warning posters and have access to Naloxone, other benzo users may not be in contact with services.

Cascaded messages to benzo users – via colleges, social media, drugs discussion groups, mental health services, GPs and public information points (libraries, health centres) are needed to reach this cohort.

- Consideration of distribution of naloxone to people who are primarily street benzo users should also be a priority even if they don't knowingly use other drugs.

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## Naloxone: nasal or IM?



**Nyoxid (nasal) or**  
**Contains 1 dose x 1.8mg/dose**  
**2 doses per distribution**

**Prenoxad (IM)**  
**contains 5 x 0.4mg doses**

There is some evidence that more doses of naloxone are required to reverse Nitazene overdoses and so Nyoxid doses may be insufficient.

Further in the event of multiple casualty events 5 doses of Naloxone + two needles allows (in extreme emergency) more people to be treated.

**Nyoxid** is slower to achieve 50% dose than IM but longer duration; this is very double edged.

Nitazenes can cause very rapid overdose and so rapid reversal is needed. So slower nasal onset times is an issue. But given the long action of isonitazene metabolites the longer action of nasal formulations is beneficial.

Further the lack of needle/barrel with nasal removes barriers to administration and the risk that kit is missing needles when needed.

**On balance where administration by injection is not a barrier, Prenoxad should be the preferred option where Nitazenes are a significant risk.**

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5836974/>

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## Naloxone Distribution and Stockpiling



- The rise of synthetics is not just a UK issue but will be a pan-European issue. Therefore there will be a significant demand on Naloxone supplies and the risk of shortages;
- It would be desirable to ensure that people were given 2-3 boxes of naloxone to ensure wider coverage and greater doses were in hand;
- Check in with those holding older kits to check that they are:
  - accessible, intact and in date
  - resupply out of date naloxone but worth keeping older stock as backup
- Ensure distribution to partner organisations especially hostels and day centres
- Make sure multiple kits are available to manage multiple overdoses in building;
- Encourage all organisations to expand beyond “999 and Naloxone” to “999 CPR and Naloxone” and distribute resus shields and/or disposable resuscitators.

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## Route changes?



- Not enough is known about different routes of administration for Nitazenes.
- Sources indicate that they can be used orally, smoked, vaped, snorted or injected.
- At present as most people are sourcing Nitazenes inadvertently as a cut in heroin they are attempting to smoke or inject it.

If Nitazenes become a market drug in their own right (e.g. people sourcing “/so”) route selection may evolve and change – with for example shifts to snorting or vaping.

- Proactive engagement with people using – “have people tried snorting it..” “*how do people get on with smoking it?*” “*Is it water soluble without an acid?*”
- This will inform our understanding of what works and what can help reduce harms if Nitazenes become an established feature.

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## Other Contaminants and Risks



Xylazine is a pharmaceutical drug used for sedation, anesthesia, muscle relaxation, and analgesia in animals such as horses, cattle, and other non-human mammals.

Xylazine has become a drug of abuse in the United States, where it is known by the street name "tranq". Is associated with skin sores and infections at injection sites.

**000232202**

Date Received: 07 Feb 2023

Postcode: NP20 -

Purchase Intent: Diazepam

Package Label: Diazepam

Sample Colour: Blue

Sample Form: Tablet

Consumption Method: Oral

Self-Reported Effects: Relaxed, Panic Attack, Insomnia, Depression

Sample Upon Analysis (Major): Bromazolam, xylazine

Sample Upon Analysis (Minor):

Click to Enlarge

Xylazine is showing up more frequently in UK heroin (yet) but is showing up in benzo-type street tablets.

There have been some reports of atypical wounds at injecting sites which may be xylazine-related.

In at least one case these were wrongly attributed to "Krokodil" (Desomorphine).

**W044469**

Date Received: 12 Dec 2023

Postcode: SE26 -

Purchase Intent: Street desomorphine

Package Label: Not Stated

Sample Colour: Pink, Brown

Sample Form: Powder

Consumption Method: Smoked

Self-Reported Effects: Increased Energy, Increased Stamina, Empathy, Relaxed

Sample Upon Analysis (Major): xylazine, Paracetamol, Caffeine

Sample Upon Analysis (Minor): Metonitazene, Isotonitazene, Heroin, Bromazolam, nitrazolam, Nicospine, 6-MAM

Click to Enlarge

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### W029473

Date Received: 16 Nov 2022

Postcode: PO7 -

Purchase Intent: THC vape liquid

Package Label: Not Stated

Sample Colour: Colourless

Sample Form: Liquid

Consumption Method: Not Stated

Self-Reported Effects: Euphoria, Relaxed, Nausea, Vomiting, Agitation, Insomnia, Depression, Erectile dysfunction

Sample Upon Analysis (Major): Metonitazene, Pregabalin, Bromazolam

Sample Upon Analysis (Minor): Nicotine, Protonitazene



Click to Enlarge

Only example of this to date. Contaminated vapes show up synthetic cannabinoids more often so this was exceptional.  
But if it becomes more common need to consider locating Naloxone in schools/colleges to provide rapid response to young people vaping.

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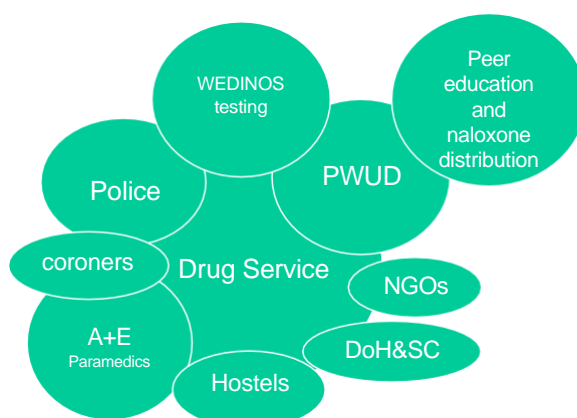
## Post non-fatal incident responses



- Support for individual to ensure well-being
- Support for those who provided help and care
- Look at opportunities for change/treatment and harm reduction
- Try and gain insight – how much was used, how used, anything unusual about batch? How prepared?
- How much naloxone required
- Any remaining drugs or syringe that could be tested?
- Cascade information to in-house working group, local groups etc

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## Developing informed local responses



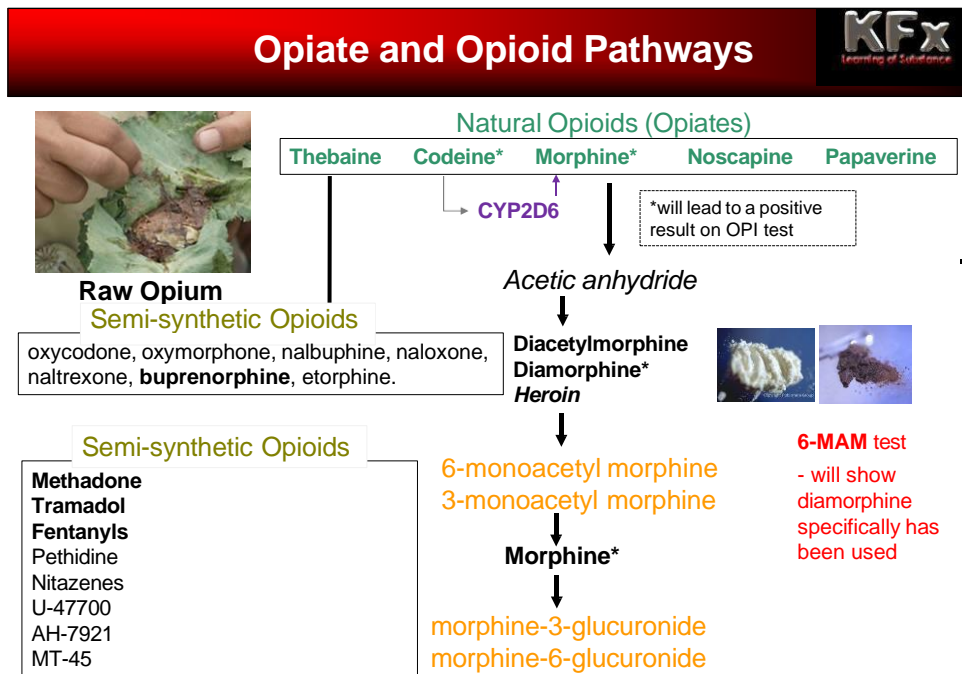
Commissioners and Drug Services could establish local response groups; Membership to include input from people who use drugs, police CD liaison officers, A+E leads, and take input from and cascade to other agencies such as hostels.

These local groups can cascade to wider national bodies such as NGOs and Third Sector organisations and to Statutory bodies such as DoH and SC.

These will help build local awareness and evidence basis, contribute to getting drugs tested, disseminate local responses and provide a credible contact point for local agencies,

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## Drug Testing

At present:

**Fentanyl**

can be detected using drug dip test and urine tests. Looking for the drugs and the main metabolite nor-fentanyl

**Xylazine**

there is a specific marketed dip test for Xylazine as a cut in drugs

**Nitazenes**

dip test available for (some) Nitazenes as a cut. Won't detect all analogues – may give false sense of security; Nitazenes can be detected by GC/MS analysis

As drug services don't routinely screen for Fentanyl (and they are not the most significant problem). We can't tell from standard urine screens if nitazenes have been used. Which leads us to several issues...

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## Testing and Treatment



### **Rejection for OST:**

Undertraining and over-reliance on a positive OPI/6-mam screen has seen some people testing negative for OPI/6-mam after claiming heroin use/dependency.

It is possible that, in some areas the lack of morphine-derived drugs in product sold as “heroin” means a negative test is possible even though opioids have been consumed.

**A negative OPI/6-mam screen should not alone be grounds for rejecting a person for OST.**

**In the current crisis, rapid access to OST is an important harm reduction measure.**

**Other markers such as clinical indicators of intoxication/withdrawal, support statements from key workers, sample drug testing and the client’s own experience should be given greater consideration than a negative test result**

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## Testing and Treatment



### **Use on top being under-reported:**

As nitazenes won’t show up in a standard OPI test or a 6-MAM test it leaves more scope for use on top of OST going unreported. This has been the case for novel benzos for a while but missed use on top introduces significant risk of OD and so need to be watchful for other markers for use on top.

### **Unknown how effective buprenorphine is against nitazenes:**

we know that at higher doses buprenorphine is effective at blocking opiate receptors against opioids with weaker binding potential (e.g. heroin).

But at present while we know that nitazenes have a high level of potency at opiate receptors we don’t know if they have a greater affinity for receptors than buprenorphine.

**If they do, then there is a reasonable chance that nitazenes will increase the risk of use on top of people prescribed buprenorphine and we should be vigilant for this risk.**

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## Hostels and DCRs



### Need rapid interventions to minimise people using alone and without support.

- Lobbying for DCRs is not going to provide the short term responses needed;
- Working with relevant hostels to ensure housing adopts high tolerance drug policies is essential
  - This will be a key element of reducing fatalities amongst vulnerably housed drug users
  - Training and joint working with hostels in overdose management
- Additional responses include wider training to public-facing services to be aware of overdose, look for naloxone on the person and aware how to use it
- Use of Apps to support people using alone is a useful adjunct but doesn't offer support 24/7, and in a time critical overdose is likely to be too slow.



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## Trauma



### Needs to be significant trauma support both for peers and workers

We are already seeing an upsurge in fatalities and sometimes multiple deaths in clusters (one locality, short time frame)

All deaths leave bereaved people and possible trauma – those who witnessed the death or tried to help

For people who are using and people in different stages of their recovery these deaths can trigger complex emotions – anger, guilt, anxiety, grief – and represent challenges to mental health and recovery.

For workers and volunteers – with or without lived experience – loss of people with whom you have worked is again traumatizing and multiple fatalities can cause significant distress.

**Organisations need to ensure bereavement and trauma support is addressed both in group and 1:1 work with people using services, and for workers and volunteers who will need support too.**

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## Looking to the future



- It's possible that Nitazenes will drop in availability but...
- There's every chance a new synthetic will follow shortly after
- My personal view is that we won't see a significant bounce back in terms of heroin in the short term and so this is a step-change in UK drug behaviours
- If we get stability we may end up with less potent Nitazenes being used in less dangerous ways
- But we may also end up with a much more dangerous, fluctuating market
- Either way local agencies have to get better at their hyper-local responses to reduce risk. Putting a poster up can never be enough.

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## Sources of Information



### **Government: Local area response tp potent opioids**

<https://www.gov.uk/government/publications/fentanyl-preparing-for-a-future-threat/guidance-for-local-areas-on-planning-to-deal-with-fentanyl-or-another-potent-opioid>

SDF Webinar (Youtube) <https://youtu.be/eSDNPaw4qQ4>

**SDF – briefings:** <https://sdf.org.uk/tag/nitazenes/>

### **ACMD review of Nitazenes**

<https://www.gov.uk/government/publications/acmd-advice-on-2-benzyl-benzimidazole-and-piperidine-benzimidazolone-opioids>

**Crew briefing:** <https://www.crew.scot/wp-content/uploads/2022/12/What-are-nitazenes.pdf>

**Wedinos:** <https://www.wedinos.org/>

### **Drug Services “collective message”**

<https://www.changegrowlive.org/news/drugs-contaminated-synthetic-opioids-collective-message>

**HIT:** <https://hit.org.uk/stayin-alive/>

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