



## Fentanyl, fentanyl analogues, and carfentanyl; Frequently Asked Questions.

What are they?

[Fentanyl](#) is a strong synthetic opioid with a rapid onset and short duration of action, used widely in medicine for pain-relief and as a general anaesthetic .

When used via parenteral (subcutaneous, intramuscular or intravenous) routes it is 100 times more potent than morphine. This means 1mg of fentanyl administered by injection has roughly the same effect as 100mg of injected morphine. By way of comparison, an intravenous (IV) dose of pure heroin (diacetylmorphine) is 'only' three times as potent as the same weight of IV morphine.

More than 40 [analogues of fentanyl](#) have been synthesized. Many are used in medicine and veterinary medicine, but some have never been used except in laboratory research. These different analogues of fentanyl are of varying potency, but most are significantly stronger than morphine by weight.

[Carfentanyl](#) (aka carfentanil) is the strongest analogue of fentanyl commercially available. A dose of carfentanyl is 10,000 times more potent than the same quantity of morphine. It's only legitimate use outside of laboratory research is as a general anaesthetic agent for large animals, such as elephants.

How do they work?

Fentanyl and its analogues [work](#) in the same way as traditional opiates and opioids, (such as morphine, heroin, and oxycodone), as an [agonist at the mu \( \$\mu\$ \) opioid receptors](#).

How are they taken?

Fentanyl and its analogues (including carfentanyl) can readily be absorbed through injection, ingestion, inhalation, across mucous membranes, *and* via transdermal (through the skin) routes.

There are a variety of prescription-only medicines containing fentanyl or its analogues, including trans-dermal patches, lollipops and nasal sprays, and ampoules for injecting use. These products are sometimes diverted to the black market. Illicitly-produced fentanyl analogues may be sold online as research chemicals or may be "cut" into black-market heroin to increase its potency.

How big a problem are they in Australia?

In Australia, fentanyl is sometimes extracted from pharmaceutical products (especially transdermal patches) by people who use drugs for purposes of injection, and a small but increasing proportion of opioid overdoses in Australia each year involve [fentanyl diverted from medical use](#) in this way.

Heroin that has been laced with illicitly produced fentanyl is called "China White". Over the last few years [fentanyl-laced heroin](#) and [counterfeit pharmaceutical pills](#) containing [fentanyl analogues](#) have



become a [significant issue](#) in North America and the EU; (for example in [Massachusetts](#) last year 75% of opioid-related fatalities involved illicit fentanyl; in Canada in 2015 the [B.C. Fentanyl Urine Screen Study](#) found nearly 29% of participants tested positive for fentanyl, even though 73% of those participants who tested positive did not report using fentanyl within the previous three days. In recent years authorities in the [EU](#) states have also been detecting samples of heroin that have been laced with fentanyl analogues, and (in the last 12 months) have detected some samples of inert powder laced with fentanyl analogues but sold to the consumer misrepresented as white (salt) heroin).

On several occasions in the past 5 years fentanyl analogues and other synthetic opioids have been detected by Australian Customs and Border Protection, and recently an importation of carfentanyl was detected entering [Queensland](#).

To date there has only been one confirmed batch of fentanyl-laced heroin (“China White”) detected in Australia. (See this forensic [case series](#) by Luke Rodda et al). However drugs seized by police represent a very small sample of drugs available in the community, and in most jurisdictions in Australia only a small proportion of drugs seized by police are subjected to serious toxicological examination. It is quite possible that other batches have not been detected.

Australia’s geographic proximity to the primary source of high-quality salt heroin in Myanmar, and our geographic isolation from traditional North American and Latin American sources of black-market fentanyl, appear to have been protective in the past. There is no evidence as yet that this is a serious issue in Australia but the cases identified by [Rodda et al](#) may be the start of an emerging trend.

The black market, like the legitimate market, is increasingly globalising. The emergence of Chinese “grey-market” labs and dark web vendors means anyone can source obscure chemicals, (or even have entirely novel substances synthesised to order), and have them shipped anywhere on the planet. The appeal to major trafficking syndicates of a product like carfentanyl is obvious. It can be sourced more cheaply (per equivalent dose) than heroin; it is roughly 1/3,300th the bulk of a dose-equivalent weight of heroin; and sniffer dogs and ion-tracking equipment will not detect it. Once imported it could be bulked out with poorer quality heroin (or even an inert powder) to turn an insignificant pinch of dust into thousands of street-deals. To major traffickers, the risk of interdiction or arrest are significantly lower and the potential profit margins are much higher.

The Chinese Government’s [recent announcement](#) that it will ban the production of carfentanyl is welcome news, but [is unlikely to significantly affect](#) the broader black market trend towards novel, highly potent synthetic drugs.



What information do NSP and other frontline workers need to know about them?

Many factors besides purity and potency influence overdose rates, however there are some indicators from anecdotal report that *could* be warning signs of heroin laced with fentanyl or other potent synthetic opioids.

- If paramedics report a spate of apparent heroin overdoses in which mega-doses of naloxone are required to reverse respiratory depression, we should suspect that a batch of heroin may have been laced with more potent opioids, (especially if these overdoses occur close in time to each other and/or in a geographically constrained area).
  - Similarly, when paramedics or drug users report an emerging pattern of incidents involving multiple people “dropping” simultaneously at one location shortly after injecting heroin, this may also be an indicator.
  - Finally if a heroin user reports significant variation in the effect of consistent, measured “tastes” that all come from the same deal of heroin, this may indicate a more potent substance that is not evenly mixed through the deal.

None of these signs is “proof” of ‘China White’.

However this does emphasise the importance of timely information sharing between different agencies and jurisdictions within Australia. And it reinforces the necessity of peer-education programs that teach drug users how to avoid overdose, how to promptly recognise the signs in others, how to respond as a first-aider (including how to administer naloxone), and to not hesitate to call an ambulance.

See also; “Minimising risk to First-aiders” and “Harm Reduction Information”, below.

Is it true that this is the drug that killed Prince? Does a high profile moment like that have an effect on usage in Australia?

The [autopsy report](#) simply stated that Prince had died of a fentanyl overdose. The full toxicology report has not been released; however media sources claim fentanyl was detected, along with lidocaine, alprazolam and oxycodone.

Prince had previously acknowledged experiencing problems with OxyContin and Percocet (initially prescribed to him following an injury). Both these medicines contain the synthetic opioid oxycodone. Prince had allegedly been treated for an opioid overdose less than a week before his death. Pills labelled hydrocodone (another synthetic opioid) were found in his home after his death, but testing showed these were counterfeit and actually contained fentanyl.

It is probable that Prince did not know he was taking fentanyl, and that these counterfeit pills, possibly in combination with prescribed oxycodone and alprazolam, (a benzodiazepine better known as Xanax), were responsible for his death.

There is no evidence that high-profile incidents like this have any significant impact on drug-using trends in the broader community.



Are these drugs that have risen in recent times, or have they been around for a while?

Fentanyl has been used in medicine since the early 1960s, and is one of the most commonly prescribed synthetic opioid in the world. A number of fentanyl analogues are quite widely used in medicine. Although the global availability of illicit fentanyl analogues and the number of fentanyl-related deaths have markedly increased in the last few years, fentanyl and other synthetic opioids have sporadically appeared on the black market in the US and some EU nations since the [late 1970s](#).

There are a number of fentanyl analogues and other synthetic opioids (such as [U-47700](#), U-50488, MT-45) that have never been used in medicine and which have recently emerged on the black market via online vendors. Some of these have never been used outside of laboratory studies, and some have never been studied or have only recently been synthesized by black market chemists. Compared to synthetic opioids that have been used in medicine, knowledge about the metabolism and toxicology of these substances is extremely limited.

My understanding is that carfentanyl is the most dangerous fentanyl analogue, with a very small dosage being potentially lethal for a human. Is that correct?

Although never tested in humans, a lethal dose of carfentanyl is probably ~20mcg ( $\mu$ g or mcg = microgram).

20mcg = 0.02mg (milligrams).

For comparison, the lethal human dose of pharmaceutical-grade fentanyl is 2mg, and a lethal dose of morphine is usually calculated as 200mg, (although doses as low as 60mg have killed opioid naïve people).

20mcg of carfentanyl would be roughly the size of a small grain of salt. Imagine crushing a small grain of salt to a fine powder, or dissolving it in a unit of water, and you can visualise how easily someone could be exposed to a dangerous dose unknowingly.

If the drug presents as a fine powder or as a solution, a quantity that is unnoticeable could easily lead to dangerous exposure via inhalation or accidental ingestion, eg: unwittingly transferred from finger-tip to mouth. The eye is another potential entry point. The fact that fentanyl analogues are readily absorbed across the skin means that even touching a small quantity of carfentanyl could be dangerous. When veterinarians handle carfentanyl they wear protection that is pretty close to a full HazMat suit.

In most first-aid situations the risk to first responders should be reasonably low, however carfentanyl is an extremely dangerous substance and first aid emergencies frequently create chaos. First responders could conceivably come into contact inadvertently with traces of substances spilled on surfaces or on the patient's skin or clothes. Drug-using peers who respond to a friend's OD are perhaps more likely to try and clean up any drugs, paraphernalia or residue before authorities arrive. This means they may be at higher risk of accidental exposure than paramedics or non-using friends or family members.

**Minimising risk to first-aiders;**

In response to a suspected exposure to potent synthetic opioids;

- Triple zero should be called immediately and first-aid administered as per an opioid OD.
- Avoid handling any drug material or paraphernalia at the scene.
- Wear nitrile or latex gloves and use a face-shield if available. As a last resort a simple face shield can be improvised from a piece of plastic bag with a hole in the centre.
- Ongoing ventilation and multiple doses of naloxone may be required.
- If inhalation exposure is suspected ensure the victim has fresh air.
- If ingestion is suspected and the victim is conscious they should be encouraged to flush their mouth, eyes and nose with fresh running water.
- If contact exposure is suspected and the person is conscious, flush the area under running water. However this will probably only help within a very short time of the contact.

**Harm Reduction Information for Fentanyl and other potent synthetic opioids.**

As mentioned above, pharmaceutical fentanyl is sometimes diverted and used in a non-medical fashion. Drug users might also source fentanyl or other synthetic opioids by ordering online from a Research Chemical vendor, or they might unknowingly be exposed to fentanyl or other potent opioids which have been “cut” into heroin.

**1) Diverted pharmaceutical fentanyl products;**

When pharmaceutical products are used in a non-medical fashion, the substance, the purity and the dose are usually known to the user. However the most easily sourced pharmaceutical products are not designed for injecting use.

Transdermal patches:

If people are misusing fentanyl patches, it is important that they know how to calculate an appropriate dose. AIVL have an excellent [“not-for-general-distribution”](#) guide to injecting fentanyl extracted from transdermal patches.

Ampoules;

Fentanyl for injection comes in ampoules with the dose in mcg/ml printed on the side. The most common is fentanyl citrate, 50mcg/ml in a 2ml amp.

50mcg = 0.05mg. This is equivalent to 50mg of morphine.

A 2ml amp at 50mcg/ml is as strong as a 100mg IV morphine.

Pharmaceutical fentanyl also presents as sublingual tablets (for breakthrough pain) lollipops (for end-of-life palliative care) and as an intranasal spray (often used in small children, or by paramedics).



**2) Fentanyl or fentanyl analogues, other novel potent opioids, imported from online vendors as research chemicals;**

The main risk with such potent substances is that it is impossible to accurately judge dose by eye, and it is impossible to accurately titrate doses by weight, (without access to scales that cost >\$10,000).

The only way to accurately measure a dose in micrograms is volumetric dosing. If a known quantity of the substance is thoroughly dissolved in a known volume of water or other solvent, measured volumes of the solution can be titrated with confidence that each dose will be the same strength. This is only safe if the person is confident of the identity of the substance and the weight of the batch. Some online vendors may misrepresent the substance they are selling, or may deliver larger or smaller amounts of the drug than expected. No matter what solvent is used, if the resulting solution is stored for any length of time there will be some evaporation, which means the solution will gradually become stronger (more concentrated).

### 3) "China White" and Heroin laced with more potent opioids;

“China White” is a name for heroin that has been laced with small amounts of fentanyl or other synthetic opioids to boost the potency. This is the most dangerous way a drug user might be exposed to fentanyl analogues or other novel potent opioids, because without access to a laboratory, there is no reliable way to detect that the adulterant is there.

The traditional advice we offer when someone is unsure of how strong a deal of heroin might be is to test a small sample first; "two holes in the arm are better than one hole in the ground". However, when a fentanyl analogue is mixed into heroin, only a speck or two difference could mean that one half of the packet is tens or even hundreds of times stronger than the other.

The best advice for individual users is to avoid using alone, and to stagger their use (ie take it in turns and wait long enough to ensure the first person is okay before injecting their own dose), or to use in a medically-supervised setting if one is available.

On a systems and policy level, Australia desperately needs to set up some form of national [EWS](#). On a service delivery and policy level, increasing heroin users' access to expired-air-resuscitation/Basic Life Support training and increasing the [availability of naloxone](#) could help to reduce the mortality and morbidity associated with "China White".

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WASUA acknowledges and respects the traditional Aboriginal and Torres Strait Islander custodians of the lands and seas on which we work, the first people of this country. We pay our respects to them, their culture, and their Elders past, present and future.

