

# Fact Sheet: Fentanyl and Synthetic Opioids



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## Questions answered in this fact sheet:

1. What is the difference between opiates and synthetic opioids?
2. What are fentanyl and fentanyl analogues?
3. How are prescription fentanyl and other synthetic opioids used in medical settings?
4. Why are illicitly-manufactured fentanyls and synthetic opioids risky to use?
5. What role are illicitly-manufactured fentanyls and synthetic opioids playing in the overdose crisis?
6. Who is at risk of illicitly-manufactured fentanyls and synthetic opioid-involved overdose?
7. How did illicitly-manufactured fentanyls and other synthetic opioids get into the illicit heroin and other drug supply?
8. How common are illicitly-manufactured fentanyls and other synthetic opioids?
9. Are illicitly-manufactured fentanyls and synthetic opioids legal?
10. What's a harm reduction approach to the use of illicitly-manufactured fentanyls and other synthetic opioids?

### 1) What is the difference between opiates and synthetic opioids?

**Opiates** are substances made from several species of the opium poppy plant that help relieve pain. These plants have been cultivated and used by humans for medicinal and recreational purposes over thousands of years.<sup>1</sup> Morphine and heroin are well-known examples of opiates.

**Fully synthetic opioids** are man-made substances in laboratories that can also relieve pain. However, 'opioid' is an umbrella category that can be used to

include plant-derived opiates, semi-synthetic opioids such as oxycodone which have compounds from plant sources and those that are made in laboratories.

### 2) What are fentanyl and fentanyl analogues?

**Fentanyl** is perhaps the most well-known of the synthetic opioids, since it has been extensively researched and is approved for prescription use. Discovered in the 1960's, fentanyl was only used for surgery, but its clinical use expanded in the 90's when an extended release skin patch was developed as treatment for chronic pain.

**Fentanyl analogues** have been designed to mimic fentanyl but have a slightly different chemical structure so they may have different effects. Following the discovery of fentanyl, some of its analogues were developed and brought to market for medical use, but recently many related compounds have been appearing on the illicit market that have no prior use in medicine. These new drugs fall into the category of novel psychoactive substances (NPS). Unfortunately, not much is known about the effects of numerous fentanyl analogues and more research is needed.

### 3) How are prescription fentanyl and other synthetic opioids used in medical settings?

They are most often used for pain relief from severe pain and under the supervision of a doctor.

Opioids are a widely researched class of drugs whose effects are well understood. In general, these effects include pain relief and sedation, but also constipation, nausea, and respiratory depression, including: shallow breathing, lowered blood pressure and reduced heart rate.<sup>2</sup> Opioids produce these effects through acting on the mu-opioid receptor in the brain.

Fentanyl is one of the most potent opioids approved for medical use, intended for chronic pain patients who have developed a tolerance to less potent opioids such as oxycodone or morphine and are no longer achieving therapeutic pain relief. Fentanyl is also used for some surgical procedures because it can be used in smaller doses than other opioids and it is faster-acting and its effects are more short-lived.

Though diversion of prescription fentanyl has occurred since it first became available, this has never been a major contributor of the increasing supply of fentanyl on the illicit market.<sup>3</sup>

Fentanyl, fentanyl analogues, and other synthetic opioids are increasingly being produced in underground laboratories. These are often referred to as illicitly-manufactured fentanyls (IMFs) and synthetic opioids. They are now commonly-used as cutting agents to street heroin and other drugs.

#### **4) Why are illicitly-manufactured fentanyls and synthetic opioids risky to use?**

Since illicitly-manufactured fentanyls and synthetic opioids are unregulated, they are of unknown composition and potency which can make it difficult to determine appropriate dosage to avoid unintentional overdose and other harms.

Many are highly potent, with effects active at much lower doses (around 1-2 nanograms or less) than other opiates.<sup>4</sup>

When added to other unregulated drugs like heroin or counterfeit prescription opioids, IMFs and other synthetic opioids can increase overdose risk dramatically. They can cause sedation and suppress breathing very rapidly so even those with a tolerance for heroin are at risk, and the risk is even greater for opioid-naïve users.

Some synthetic opioids are known only by their chemical shorthand, such as W-18, U-47700 and AH-7921. Potency and effects can vary widely among these substances, and short and long term health risks are not always clearly known because they are difficult to study and are often emerging in drug markets faster than they can be tracked.

#### **5) What role are illicitly-manufactured fentanyls and synthetic opioids playing in the overdose crisis?**

Recent estimates suggest that over 94,000 people died of drug overdose in the 12-month period leading up to January 2021 and 60% of these involved illicitly-manufactured fentanyls or other synthetic opioids.<sup>5</sup>

Illicitly-manufactured fentanyls and synthetic opioids first were involved in overdose deaths in midwestern and eastern states and the age-adjusted overdose death rate involving these substances increased by an average of 75% every year between 2013 and 2017.<sup>6</sup> Their involvement in overdose deaths has expanded to states west of the Mississippi and increased in the majority of states since 2019.<sup>7</sup>

At the same time, cocaine-involved overdose deaths have tripled since 2012 and methamphetamine-involved overdose deaths have increased sixfold.<sup>8</sup> Meanwhile the involvement of heroin and prescription opioids in overdose deaths has remained stable or decreased in many regions.<sup>9</sup>

#### **6) Who is at risk of illicitly-manufactured fentanyl- and synthetic opioid-involved overdose?**

People at highest risk of fatal overdose involving illicitly-manufactured fentanyls and synthetic opioids are those who use illicit drugs such as heroin, counterfeit prescription opioids or benzodiazepines, or in rare cases other drugs because they may be unknowingly adulterated or cross-contaminated with IMF or synthetic opioids.

The higher potency means their effects are stronger at lower doses than the heroin or counterfeit pills they may be mixed in. Thus, if people who stop using heroin then return to heroin use, their tolerance has inevitably been lowered, and they are more susceptible to overdose.<sup>10</sup> Moreover, even in people already using heroin, their tolerance to stronger synthetic opioids like fentanyl may be lower,<sup>11</sup> so risk of accidental overdose is higher if they unknowingly take fentanyl-laced heroin, whether through the same method, or their first time trying a new method (i.e. snorting, smoking, or injecting).<sup>12</sup>

## **7) How did illicitly-manufactured fentanyl and other synthetic opioids get into the illicit heroin and other drug supply?**

Illicitly-manufactured fentanyl and synthetic opioids were initially introduced into east coast and midwest heroin supplies because these substances were viewed as an attractive cutting agent, since their increased sedative potency can be perceived as strengthening a batch of heroin and it mixed well into the characteristic “china white” heroin available in these regions.<sup>13</sup>

Due to prohibition, there is more incentive for producers and distributors to minimize costs and maximize profits, while avoiding law enforcement detection. This is referred to as The Iron Law of Prohibition and has been used to explain why illicitly-manufactured fentanyl entered the underground opioid supply.<sup>14</sup>

Sellers in the illicit market are constantly weighing costs and profit against potency.<sup>15</sup> When cutting agents like illicitly-manufactured fentanyl and other synthetic opioids are added, this increases the quantity that can be sold. As long as a particular batch produces noticeable effects, demand will remain.

Illicitly-manufactured fentanyl and synthetic opioids have been found in counterfeit pressed pills sold as prescription opioids or benzodiazepines, and in trace amounts in batches of other drug supplies.<sup>16</sup> It is still unclear whether their presence in non-opioid drug supplies is intentional or a result of unintentional cross-contamination from shared preparation surfaces or equipment.

## **8) How common are IMFs and other synthetic opioids?**

The most reliable evidence showing the presence of illicitly-manufactured fentanyl and synthetic opioids in the illicit drug supply comes from reports by the U.S. Drug Enforcement Administration (DEA) which contain information on drug seizures and analyses from the National Forensic Laboratory Information System (NFLIS).<sup>17</sup>

In 2019, they determined that availability was high across the country in the majority of the DEA’s Field Divisions, and reports of illicitly-manufactured fentanyl in the NFLIS increased by 12% between 2018 and

2019.<sup>18</sup> Seizures predominantly occurred along the southwest border and were recorded in states with high heroin seizures as well since those markets are interconnected, including the Mid-Atlantic, Great Lakes, and Northeast regions. However, illicitly-manufactured fentanyl and synthetic opioids have been increasingly detected in counterfeit prescription pills in states across the country as well.

The DEA’s Special Testing and Research Laboratory’s (STRL) Fentanyl Signature Profiling Program (FSPP) data suggests that illicitly-manufactured fentanyl is rarely mixed into the heroin supply at the wholesale level, but likely at the regional and local level.<sup>19</sup> The FSPP has also determined that the majority of illicitly-manufactured fentanyl found in the country are sourced from Mexico and those sourced from China have rapidly declined in recent years.

## **9) Are illicitly-manufactured fentanyl and synthetic opioids legal?**

In the United States, fentanyl is classified as a Schedule II controlled substance, meaning there is a potential for misuse and dependence, but it does have an accepted medical use and can be prescribed for restricted use.

In 2016, following the high profile case of music legend Prince’s fentanyl-related death and increasing seizures of illicitly-manufactured fentanyl by law enforcement, calls from politicians<sup>20</sup> to increase punishment for possession and/or sale of illicitly-manufactured fentanyl included escalating mandatory minimum sentencing, and even capital punishment for sale of heroin.<sup>21</sup> Between 2011 and 2020, 45 states proposed or enacted new legislation to increase penalties.<sup>22</sup>

In 2018, the DEA used its emergency scheduling ability to temporarily schedule fentanyl analogues as Schedule 1 drugs, which locked in harsh penalties and mandatory minimums for people found in possession of small amounts of these drugs. The emergency scheduling was slated to expire in 2020, but was extended through May of 2021, and has been extended as of this writing through October 2021.

## **10) What’s a harm reduction approach to the use of illicitly-manufactured fentanyl and other synthetic opioids?**

The first, most important step is to increase access to,

and continue to develop accurate, non-judgmental education programs on safer drug use and overdose prevention strategies. Important harm reduction strategies include: never use alone; don't mix opioids with other depressants like alcohol and benzodiazepines; keep naloxone on hand; use drug checking equipment such as fentanyl test strips, and others.

There are also a number of policies that should be expanded to promote a public health approach to the presence of illicitly-manufactured fentanyls and synthetic opioids in the supply:

1. Expand and protect 911 Good Samaritan laws,
2. Expand community-based naloxone access and distribution,
3. Expand Opioid Agonist Treatment (OAT),
4. Improve drug checking, surveillance and data collection and make them more widely accessible,
5. Authorize Overdose Prevention Centers (OPC) on the state and local level,
6. Fund pilot injectable opioid treatment as an option for some people with chronic heroin use disorder.

Drug Policy Alliance (DPA) has put together recommendations for a comprehensive response to the overdose crisis that includes these harm reduction initiatives as well as others.<sup>23</sup> DPA also works to ensure these life-saving strategies don't meet with political resistance. When it comes to fentanyl and other synthetic opioids, we must ensure that any new laws do not imitate ineffective drug war tactics by relying on criminal punishment rather than a public health approach.

<sup>1</sup> "Erowid Opiates Vault : Opium Timeline." Erowid Opiates Vault : Opium Timeline. [https://www.erowid.org/chemicals/opiates/opiates\\_timeline.php](https://www.erowid.org/chemicals/opiates/opiates_timeline.php).

<sup>2</sup> Stott, D. G., and B. J. Pleuvry. "Relationship Between Analgesia And Respiratory Depression For Mu Opioid Receptor Agonists In Mice." *Br J Anaesth BJA: British Journal of Anaesthesia* 67, no. 5 (1991): 603-07. doi:10.1093/bja/67.5.603.

<sup>3</sup> U. S. Department of Justice, Drug Enforcement Administration, DEA Investigative Reporting, January 2015

<sup>4</sup> Peng, Philip W. H., and Alan N. Sandler. "A Review of the Use of Fentanyl Analgesia in the Management of Acute Pain in Adults." *Anesthesiology* 90, no. 2 (1999): 576-99. doi:10.1097/0000542-199902000-00034.

<sup>5</sup> Ahmad FB, Rossen LM, Sutton P. "Provisional drug overdose death counts." National Center for Health Statistics. 2021. <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>

<sup>6</sup> Hedegaard, Holly, Arialdi M. Minino, and Margaret Warner. 2020. "Drug Overdose Deaths in the United States, 1999–2019." NCHS Data Brief, no. 394: 8.

<sup>7</sup> Health Alert Network (HAN). Provided by the Centers for Disease Control and Prevention (CDC). 2020. "Increase in Fatal Drug Overdoses Across the United States Driven by Synthetic Opioids Before and During the COVID-19 Pandemic." December 17, 2020. <https://emergency.cdc.gov/han/2020/han00438.asp>

<sup>8</sup> Hedegaard, Minino & Warner. 2020.

<sup>9</sup> Ahmad, Rossen, & Sutton. 2021.

<sup>10</sup> Strang, John. "Death Matters: Understanding Heroin/opiate Overdose Risk and Testing Potential to Prevent Deaths." *Addiction* 110 (2015): 27-35. doi:10.1111/add.12904.

<sup>11</sup> Kriván, Márta, Gyula Szabó, Zoltán Sarnyai, Gábor L. Kovács, and Gyula Telegdy. "Oxytocin Blocks the Development of Heroin-fentanyl Cross-tolerance in Mice."

*Pharmacology Biochemistry and Behavior* 52, no. 3 (1995): 591-94. doi:10.1016/0091-3057(95)00145-m.

<sup>12</sup> Hall, Aron J. "Patterns of Abuse Among Unintentional Pharmaceutical Overdose Fatalities." *Jama* 300, no. 22 (2008): 2613. doi:10.1001/jama.2008.802.

<sup>13</sup> Beletsky, Leo, and Corey S. Davis. 2017. "Today's Fentanyl Crisis: Prohibition's Iron Law, Revisited." *International Journal of Drug Policy*, 46, 156-159.

<sup>14</sup> Ibid.

<sup>15</sup> Mars, Sarah G., Daniel Rosenblum, and Daniel Ciccarone. 2019. "Illicit Fentanyls in the Opioid Street Market: Desired or Imposed?" *Addiction* 114 (5): 774–80. <https://doi.org/10.1111/add.14474>.

<sup>16</sup> Drug Enforcement Agency. 2021. "2020 National Drug Threat Assessment." <https://www.dea.gov/documents/2021/03/02/2020-national-drug-threat-assessment>

<sup>17</sup> Ibid.

<sup>18</sup> Ibid.

<sup>19</sup> Ibid.

<sup>20</sup> "S.Amdt.4101 to S.2943 - 114th Congress (2015-2016) - Amendment Text." Congress.gov. <https://www.congress.gov/amendment/114th-congress/senate-amendment/4101/text>.

<sup>21</sup> Reed, Harry. "H.R.6158 - 114th Congress (2015-2016): HELP Act of 2016." Congress.gov. <https://www.congress.gov/bill/114th-congress/house-bill/6158>

<sup>22</sup> Collins, Michael, and Sheila P. Vakharia. 2020. "Criminal Justice Reform in the Fentanyl Era: One Step Forward, Two Steps Back." <https://drugpolicy.org/resource/criminal-justice-reform-fentanyl-era-one-step-forward-two-steps-back>.

<sup>23</sup> "Opioid Overdose: Addressing a National Crisis of Preventable Deaths." Opioid Overdose: Addressing a National Crisis of Preventable Deaths | Drug Policy Alliance. <http://www.drugpolicy.org/resource/opioid-overdose-addressing-national-crisis-preventable-deaths>