



# Fentanyl

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## RESEARCH IN BRIEF

- There is an average of one death every three days due to fentanyl overdose in Canada
- Death, while very serious, is only a small part of the harms associated with fentanyl
- Fentanyl is 100 times more powerful than morphine and more dangerous than heroin
- Fentanyl's effects resemble those of heroin, except far more potent
- Those using fentanyl lawfully need to be certain they are fully aware of the drug interactions
- Fentanyl use (illicit or lawful) and dangerous occupations do not mix
- Help save lives by sharing this information with your family and friends

## BRIEF DESCRIPTION

### Medical Application

Fentanyl is used to manage severe pain and post-surgery pain in medicine. Fentanyl is 100 times more powerful than morphine at the equivalent dose by weight. Fentanyl is a synthetic opiate, classified as a pain killer that is available in prescription form Actiq®, Duragesic®, Fentora®, Sublimaze® and others. Intravenous fentanyl is extensively used for anesthesia and analgesia, most often in operating rooms and intensive care units. When prescribed by a physician, fentanyl is often administered via injection, transdermal patch, or in lozenges. Fentanyl patches release slowly over 72 hours, and serve as a promising pain management tool for severe pain management and post-surgical pain management. Because of the risk of misuse, abuse, addiction, and overdose, fentanyl is available only through a restricted program required by the Food and Drug Administration called a Risk Evaluation and Mitigation Strategy (REMS). As of 2012, fentanyl was the most widely used synthetic opioid in medicine. In 2013, 1700 kilograms were used globally. Fentanyl is broadly applied in medicine; it is a very safe surgical anesthetic. Due to the extreme potency of the substance – ensuring a non-lethal dose requires special skills and high dilution.

### Non-Medical (Recreational) Use

Both pharmaceutical and non-pharmaceutical analogs of fentanyl are abused. Fentanyl from non-pharmaceutical sources is sold in the following forms: as a powder; spiked on blotter paper; mixed with or substituted for heroin; or as tablets that mimic other, less potent opioids. Synthesis of illicit fentanyl has occurred in Canada, but indicators point to a low incidence. The main illicit source is pharmaceutical grade imports of fentanyl commonly from China. Abuse occurs by swallowing, snorting, injecting, or by placing spiked blotted paper in the mouth; absorbed through the mucous membrane. Fentanyl is most commonly used orally, however, similar to heroin can also be smoked, snorted or injected. Fentanyl is sometimes sold as heroin, often leading to overdoses. In fact, many fentanyl overdoses are initially classified as heroin overdoses. Street names include apache, china white, china girl, dance fever, goodfella, and TNT. Pharmaceutical fentanyl is abused by removing the entire volume of the patch and injecting the contents as a single dose. Both of these uses are deadly.

### Dangers

Fentanyl acts on opioid receptor sites found in areas of the brain responsible for the experience of pain and emotions – the danger is that it impacts the part of the brain that controls breathing rate. High doses of opiates, notably those that are highly potent, can cause breathing to stop – which leads to death. Overdoses of fentanyl need to be treated immediately with naloxone, and may require very high doses to successfully reverse the overdose. Due to the short-lived effects of the drug, regular users become addicted very rapidly and require increasing amounts to produce the same effects. Critical issues arise due to the potency as compared to heroin, and due to the intense respiratory depression, common with anesthetics, there is a larger risk than heroin to the user.

## EFFECTS

Similar to heroin, morphine, and other opioid drugs, fentanyl acts on the body by binding to the opioid receptors in the areas of the brain responsible for the experience of pain and emotions. When opioid drugs bind to the receptors they increase dopamine levels in the brain's reward areas, resulting in a state of euphoria and relaxation. Fentanyl's effects resemble those of heroin and include euphoria, drowsiness, nausea, confusion, constipation, sedation, tolerance, addiction, respiratory depression and arrest, unconsciousness, coma, and death.

Short-Term Fentanyl Abuse	Long-Term Fentanyl Abuse Effects
<ul style="list-style-type: none"><li>• Euphoria and rapid addiction</li><li>• Respiratory (Dyspnea)</li><li>• Confusion, dizziness, drowsiness, fatigue, headache, sedation (Central Nervous System)</li><li>• Dehydration (Endocrine &amp; Metabolic)</li><li>• Constipation, nausea, vomiting (Gastrointestinal)</li><li>• Weakness (Neuromuscular &amp; Skeletal)</li><li>• Risk of death</li></ul>	<ul style="list-style-type: none"><li>• Criminal activity to support habit</li><li>• Depression</li><li>• Weight loss / loss of appetite</li><li>• Anxiety</li><li>• Tremors / withdrawal symptoms</li><li>• Tolerance requiring higher doses</li><li>• Serotonin syndrome</li><li>• Risk of death</li></ul>

Table 1.0

## INTERACTION HIGHLIGHTS

Interactions vary by the administration method and are numerous. Some of the more common and serious interactions include benzodiazepines and other Central Nervous System (CNS) depressants like cough medicines and alcohol. Fentanyl concentrations may also be increased by grapefruit juice. Concomitant use of fentanyl with cytochrome P450 (CYP-450) 3A4 inhibitors can lead to complications and death.

Other interactions are based on misuse (patient error). Errors such as exposure of the fentanyl application site and surrounding area to direct external heat sources, such as heating pads or electric blankets, heat or tanning lamps, sunbathing, hot baths, saunas, hot tubs, and heated water beds may increase fentanyl absorption and has resulted in fatal overdoses of fentanyl and death.

Consultation is a must with a licensed physician equipped with the most Up-To-Date® information on this topic as it is prudent to any medical use.

## KEY CANADIAN STATISTICAL FINDINGS

- There were 665 deaths due to fentanyl overdose, this is one death every 3 days (2007- 2014)
- There are drastic increases in post modern detection and deaths caused by, or related to, fentanyl:
  - Alberta: 14 fold increase from 2011 to 2014 (cause or contributor)
  - British Columbia: 7 fold increase from 2012 to 2014 (detected only)
  - Ontario: 1.7 fold increase from 2011 to 2013 (cause or contributor)
  - Quebec: Doubled from 2009 to 2013 (cause or contributor)
- Most identified occupational abusers are medical staff
- Alarming increase of fentanyl abuse in teens resulting in death
- 10% higher incidence of abuse in women versus men

## DETECTION

Fentanyl is detectable in urine utilizing currently available forensic testing processes. Typically fentanyl testing is performed mostly in medical monitoring programs, and on a case-by-case basis as part of recommendations by a substance abuse expert. In all cases where there are changes to the standard drug testing panel that is applied to mitigate risk for safety sensitive staff, functions and/or areas, employers are encouraged to document their rationale, update their policy, train their supervisors and inform their people. **All employers are encouraged to educate their staff on fentanyl for both their personal safety and the safety of their family, as the adverse effects of this drug can ultimately result in death.**

Fentanyl Trade Names	Known Fentanyl Analogs
<ul style="list-style-type: none"> <li>• DEA #9801 (Controlled Substances Schedule II)</li> <li>• Duragesic</li> <li>• Fentanest</li> <li>• Fentanil</li> <li>• Fentanila (Spanish)</li> <li>• Fentanylum (Latin)</li> <li>• Leptanal</li> <li>• Pentanyl</li> <li>• 1-Phenethyl-4-(N-phenylpropionamido)piperidine</li> <li>• 1-Phenethyl-4-(phenylpropionylamino) piperidine</li> <li>• N-(1-Phenethyl-4-piperidyl)propionanilide</li> <li>• N-Phenethyl-4-(N-propionylanilino)piperidine</li> <li>• 1-Phenethyl-4-N-propionylanilinopiperidine</li> <li>• Phentanyl</li> <li>• N-Phenyl-N-[1-(2-phenylethyl)-4-piperidiny]pro pan- amide</li> <li>• Propanamide, N-phenyl-N-[1-(2-phenylethyl)-4-piper- idiny]</li> <li>• Propionanilide, N-(1-phenethyl-4-piperidyl)-</li> <li>• R 4263</li> <li>• Sentonil</li> </ul>	<ul style="list-style-type: none"> <li>• 3-methylfentanyl (TMF)</li> <li>• 3-methylthiofentanyl</li> <li>• Acetyl fentanyl</li> <li>• Acetyl-alpha-methylfentanyl</li> <li>• Alfentanyl</li> <li>• Alpha-methylfentanyl</li> <li>• Alpha-methylthiofentanyl</li> <li>• Beta-hydroxy-3-methylfentanyl</li> <li>• Beta-hydroxyfentanyl</li> <li>• Butyrfentanyl</li> <li>• Carfentanyl</li> <li>• Para-fluorofentanyl</li> <li>• Remifentanyl</li> <li>• Sufentanyl</li> <li>• Thiofentanyl</li> <li>• Ocfentanyl</li> </ul>

Table 2.0

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