

Emerging Trend: Para-fluorofentanyl (pFF) Increase in Michigan 2018-2022 Year-to-Date

Highlights

Following nearly four decades of obscurity, a fentanyl analog never intended for human use is once again appearing in the illicit drug market in the United States. Para-fluorofentanyl (pFF) is an illicit synthetic opioid that was classified as a Schedule 1 drug in 1986.

This brief describes an emerging drug trend—a **sharp increase in decedents testing positive for pFF in Michigan**, identified via the Swift Toxicology of Overdose-Related Mortalities (STORM) program. STORM began in September 2017, to improve rapid toxicological testing of mortality samples in Michigan.

While STORM started testing for pFF in January 2018, the first pFF-positive death was not identified until September 2020. As of October 2022, STORM has detected 284 pFF-positive deaths, 72% of which occurred November 2021 to October 2022.

In [January 2022, a MMWR weekly report from the CDC](#)¹ highlighted an increase in decedents testing positive for pFF in Knox County, Tennessee, and recommended increased public awareness and expanded naloxone availability.

What is Para-fluorofentanyl?

Information from Michigan Poison & Drug Information Center

Para-fluorofentanyl (4-fluorofentanyl or pFF) is a Schedule I synthetic opioid analgesic first synthesized for research purposes in the 1960s.¹ pFF is a fentanyl analog (i.e., fentalog) with a similar chemical structure and synthesis route to fentanyl.² Clinical research evidence indicates **pFF is more potent than fentanyl**, which is approximately 50 to 100 times more potent than morphine.³

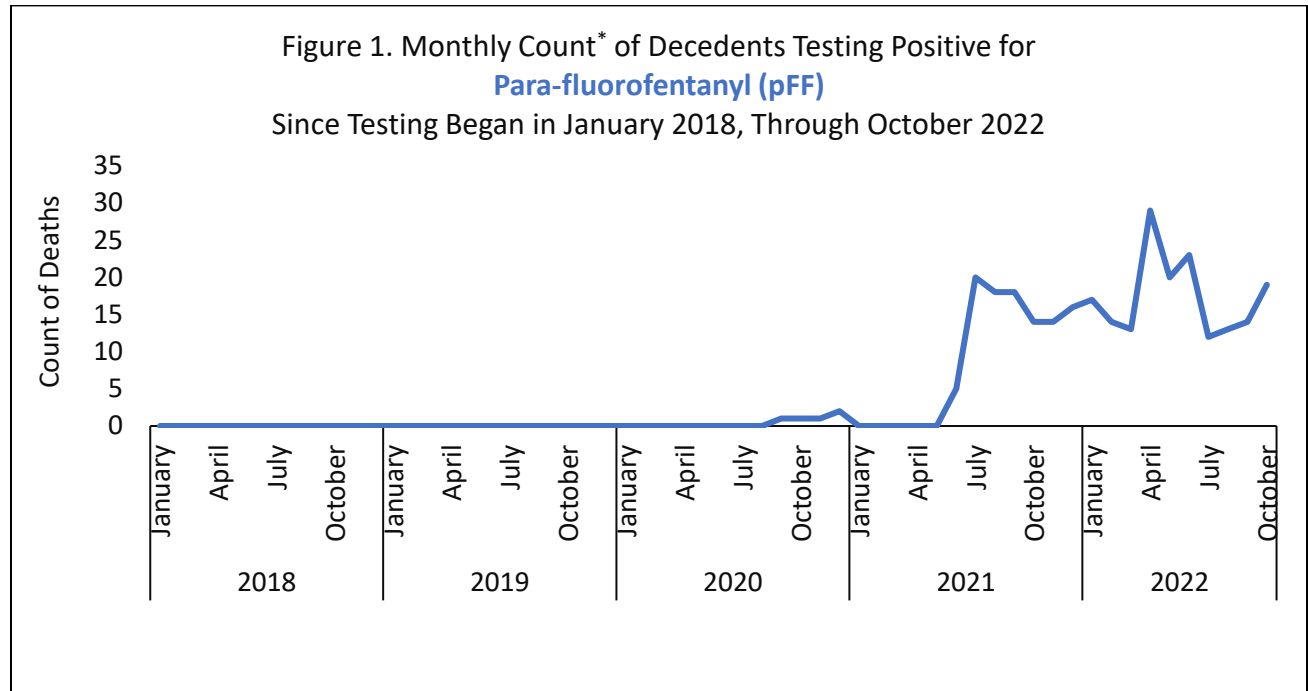
pFF was present in illicit drug supplies dating back to the early 1980s before the advent of the Federal Analog Act, which treats any chemical deemed substantially similar to a controlled substance in Schedule I or Schedule II as if it were a Schedule I substance.⁴ However, **pFF has recently reemerged in the illicit drug market**. It has been detected in heroin packets and counterfeit pills. It has also been linked to multiple overdose deaths across several US states.¹

The potency of pFF can vary between different drug supplies due to the nature of the unregulated, clandestine chemical manufacturing process. This narrows the safety threshold and misleads users, placing them at increased risk of opioid toxicity. Signs and symptoms associated with pFF overdose are like other opioid analgesics, including pinpoint pupils, central nervous and respiratory system depression, cyanosis, and coma. **Naloxone is an effective opioid reversal agent and should be administered in patients presenting with a toxic syndrome consistent with opioid overdose along with early ventilation support and oxygenation.**

Unlike other opioid analgesics (ex., heroin, morphine), **pFF is not detected during routine toxicology testing** and requires specialized forensic toxicology testing. Specialized testing has inherent limitations since results are typically not available for days, precluding effective utility in an acute clinical setting.

Detailed Findings

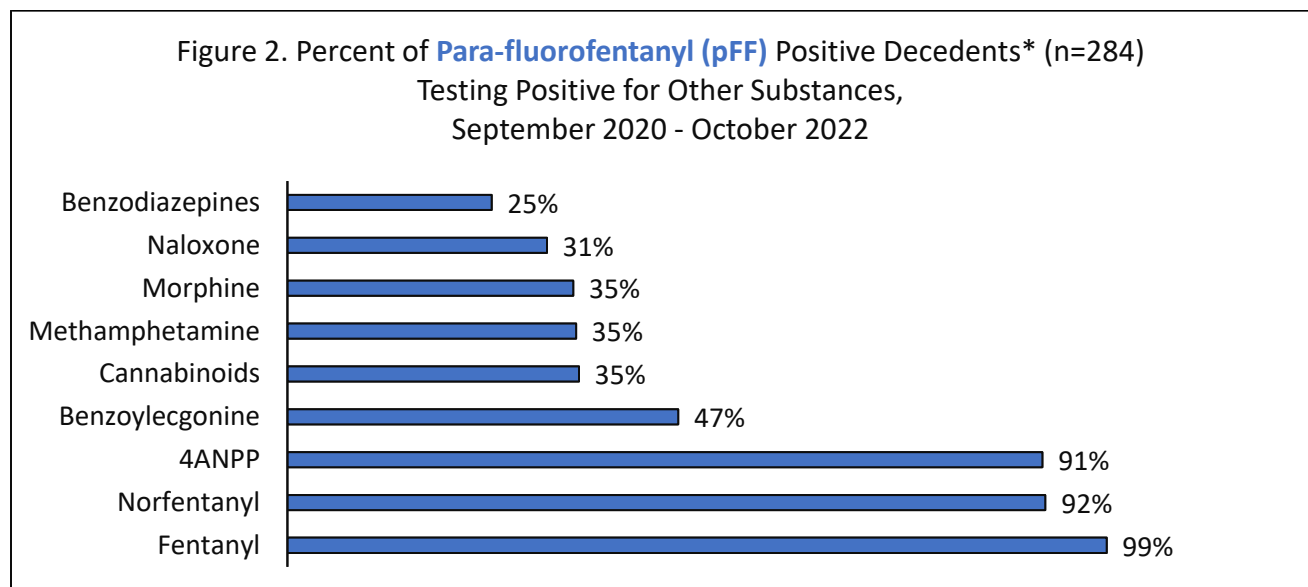
The number of pFF-positive decedents increased from five in 2020 to 105 in 2021, a 2,000% relative increase (Figure 1). From January to October 2022, STORM has detected pFF in 174 decedents. Projecting the monthly average from October to the end of 2022, STORM could see an annual count of 209 pFF-positive decedents, a 99% relative increase from 2021.



**2020-2022 The Swift Toxicology of Overdose-Related Mortalities (STORM) Program at Western Michigan University Homer Stryker MD School of Medicine (WMed)*

Of decedents testing positive for pFF (Figure 2), commonly co-occurring substances were:

- Benzoyllecgonine, a metabolite of cocaine, 47% (134/284); and
- Methamphetamine, 35% (99/284).



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Of decedents testing positive for pFF in STORM:

- 32% were female, and 65% were male;
- 20% were Black/African American, and 77% were white;
- 57% were between ages 30-49.

In July 2022, STORM identified two pFF-positive decedents under the age of 5, an unprecedented occurrence in STORM and in retrospective, abstracted death records from January 1, 2020 to January 31, 2022. The deaths occurred in Oceana County, Michigan, and St. Joseph County, Indiana, a bordering county which participates in the STORM Project. Local Children’s Protective Services were contacted in both cases.

Of all pFF-positive decedents, deaths have occurred in 23 Michigan counties and 2 counties in Northern Indiana. Most deaths occurred in: Genesee (60), Ingham (52), and Muskegon (29) counties, representing 50% of all pFF deaths.

How You Can Act

Get the message out. pFF is an illicit opioid increasingly found in the drug supply in Michigan and using it alone or in combination with other opioids, like fentanyl, can cause a fatal overdose.

Educate about the signs of opioid overdose and how to use naloxone to reverse an opioid overdose. Train bystanders to use naloxone and, in cases where naloxone is not available or is not working yet, to use CPR, rescue breathing, and/or chest compressions to sustain life until EMS arrives. Additional doses of naloxone may be required to reverse the effects of pFF and fentanyl ([MMWR](#)).

Distribute naloxone. Organizations can [request free naloxone from MDHHS](#) to increase capacity. Connect individuals with more ways to access naloxone: order online at [nextdistro.org/Michigan](#) and have it delivered at no cost; get it at a pharmacy ([Naloxone Standing Order](#), no prescription required); or contact a [Syringe Service Program](#) for naloxone, fentanyl test strips, sterile needles, testing for HIV and Hepatitis C, and other life-saving resources.

Promote harm reduction messages. “Assume overdose risk no matter what drug you are using, and practice as much harm reduction as possible, as consistently as possible: Go slow. Use less. Test your product. If you are using alone, double down on other strategies. Have someone check on you. Smoke or snort instead of inject. If you are using in a group, stagger your use so someone is always alert. Know the signs of an overdose. Carry naloxone and know how to use it. Look out for each other!” ([Fentanyl Use and Overdose Prevention Tips - National Harm Reduction Coalition](#)⁵).

Technical Notes

Data Source: STORM Project Dataset (2017-2022), updated by WMed, November 29, 2022.

Limitations: Because the number of counties participating in STORM and the number of substances or analogues being tested can change, caution should be exercised when interpreting this data. This data cannot definitively state the burden of any particular opioid or analogue within the state of Michigan or any specific county. Due to limited death information, it is impossible to determine whether a positive drug result in this project is indicative of drug toxicity or was a contributing cause of death.

References

1. Trecki J, Gerona RR, Ellison R, Thomas C, Mileusnic-Polchan D. *Notes from the Field: Increased Incidence of Fentanyl-Related Deaths Involving Para-fluorofentanyl or Metonitazene – Knox County, Tennessee, November 2020-August 2021*. MMWR Morb Mortal Wkly Rep 2022;71:153-155. DOI: <http://dx.doi.org/10.15585/mmwr.mm7104a3>
2. Mounteney J, Giraudon I, Denissov G, Griffiths P (July 2015). "Fentanyls: Are we missing the signs? Highly potent and on the rise in Europe" *The International Journal on Drug Policy*. **26** (7): 626–31.
3. Papsun et al. Fluorofentanyl Identified in Forensic Casework as Wave of Fentanyl-Related Substances Appears in the United States. NPS Discovery, CFSRE. December 2020.
4. Henderson GL (March 1988). "Designer drugs: past history and future prospects". *Journal of Forensic Sciences*. **33** (2): 569–75.
5. The DOPE Project. Fentanyl Use and Overdose Prevention Tips. National Harm Reduction Council. Accessed August 18, 2022. [Fentanyl Use and Overdose Prevention Tips - National Harm Reduction Coalition](#)

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