

The Rise of Brorphine — A Potent New Synthetic Opioid Identified in the Midwestern United States

Purpose: The objective of this announcement is to notify public health and safety, law enforcement, first responders, clinicians, medical examiners and coroners, forensic and clinical laboratory personnel, and all other related communities about new information surrounding the emergent synthetic opioid **brorphine**.

Background: Synthetic opioids are chemically manufactured drugs, often accompanied with unknown potency and adverse effects or health risks. New synthetic opioids may be mixed with more traditional opioids, creating additional risk and danger for recreational drug users. Synthetic opioids may be distributed in powder or tablet form. In the United States (U.S.), an alarming increase in the number of deaths linked to synthetic opioid use has been reported. The primary adverse effect associated with synthetic opioid use is respiratory depression, often leading to death.

Summary: Our laboratory previously reported the appearance of the potent synthetic opioid **isotonitazene** on the illicit drug market in late 2019. Data from controlled substance testing showed drug materials containing isotonitazene appeared as gray granular powder, often in combination with **flualprazolam**, an illicit benzodiazepine. In June 2020, the U.S. Drug Enforcement Administration (DEA) temporarily scheduled isotonitazene. Shortly thereafter, detections of **brorphine** in the U.S. began to increase, appearing as similar gray drug powders and an apparent replacement for isotonitazene. Brorphine is a potent synthetic opioid with structural resemblance to fentanyl and its analogues. However, brorphine is not controlled in the U.S. under core-structure scheduling of fentanyl related substances. Brorphine was first synthesized and reported in 2018, although analogues of brorphine appear in scientific literature as far back as the 1960s. *In vitro* pharmacological data show brorphine exhibits potency similar to fentanyl. Recent detections in drug related deaths leads us to believe this new synthetic opioid has the potential to cause widespread harm and is of public health concern. As of mid-July 2020, brorphine was confirmed in seven blood specimens associated with fatalities in the U.S.; brorphine has also been reported in Europe (Belgium).

Brorphine Related Deaths Demographics

Age:

- Avg. 52, Med. 53
- Range: 40's to 60's

Sex:

- Male (n=6), Female (n=1)

Case Type:

- Postmortem (n=7)

Specimen Type:

- Blood (n=7)

Date of Collection:

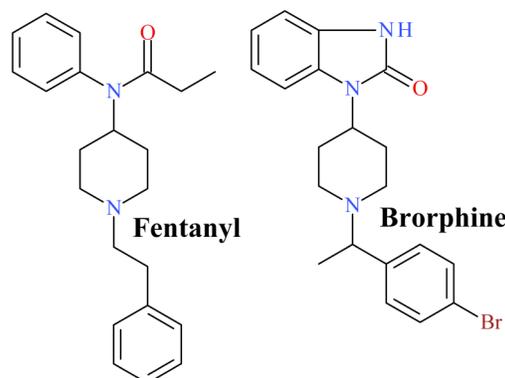
- June to July 2020

Other Notable Findings:

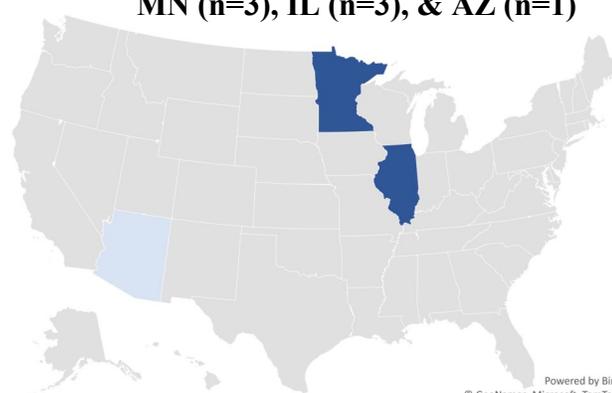
- Fentanyl (n=7)
- Flualprazolam (n=5)
- Heroin (n=4)

Recommendations for Public Health

- Implement surveillance for rapid identification of drug overdose outbreaks.
- Engage local poison centers and clinicians to assist with treatment of affected patients.
- Track and monitor geographical drug distribution and trends.
- Track demographics and known risk factors for decedents and overdose patients.
- Raise awareness about the risks and dangers associated with opioid use.
- Make naloxone available to recreational drug users.



MN (n=3), IL (n=3), & AZ (n=1)



Recommendations for MEs & Coroners

- Test for new synthetic opioids and their biomarkers in suspected opioid overdose cases.
- Be aware that ELISA screening for synthetic opioids may not be specific or specialized for the newest generation of compounds; consider mass spectrometry-based screening.
- Be aware that concentrations of synthetic opioids in biological specimens can vary and GC-MS sensitivity may not be adequate.

Recommendations for Clinicians

- Become familiar with the signs and symptoms associated with synthetic opioid use (e.g. sedation, respiratory depression).
- Naloxone should be administered to reverse critical respiratory depression and repeated naloxone administration may be necessary. Be aware that clinical conditions may change rapidly and unpredictably after naloxone administration due to precipitation of withdrawal.
- Be mindful that illicit drugs have limited quality control, containing undeclared substances that impact the expected clinical effects or findings.
- Counsel about the dangers of synthetic opioid products and other drugs.

Recommendations for Laboratories

- Utilize analytical data available publicly for the identification of brorphine and other synthetic opioids if reference standards are not available.
- Utilize previously developed non-targeted testing protocols or develop sensitive and up-to-date testing procedures for synthetic opioids.
- Prioritize analytical testing of seized drug samples taken from drug overdose scenes during death investigations.
- Share data on synthetic opioid drug seizures with local health departments, medical examiners, and coroners.

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References and Related Articles:

- Kennedy et al. (2018) *Optimization of a series of mu opioid receptor (MOR) agonists with high G protein signaling bias.* *Journal of Medicinal Chemistry*, 61, 8895-8907.
- Verougstraete et al. (2020) First report on brorphine: the next opioid on the deadly new psychoactive substances' horizon? *Journal of Analytical Toxicology*. [Epub ahead of print]
- CDC: [Synthetic Opioid Overdose Data](#)

Rapid NPS Testing Now Available:

If your agency suspects synthetic opioid toxicity with no identifiable cause of death or your jurisdiction is noticing an increase in overdose patients requiring analytical testing, contact NPS Discovery at the Center for Forensic Science Research and Education; a non-profit organization in collaboration with DOJ and CDC, which has received funding to provide rapid testing of novel drug outbreaks in the United States.

Website: npsdiscovery.org Email: npsdiscovery@cfsre.org