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Flualprazolam: Potent Benzodiazepine Identified Among Death and Impaired Driving Cases in the U.S.

Purpose: The objective of this public announcement is to notify public health and public safety officials, law enforcement, clinicians, medical examiners and coroners, laboratory personnel, and all other related communities about information surrounding the emergent benzodiazepine flualprazolam — a novel psychoactive substance (NPS).

Background: NPS benzodiazepines, sometimes referred to as designer benzodiazepines, are synthetically manufactured drugs, often associated with unknown biological effects and health risks, a dangerous combination for any recreational drug user. NPS benzodiazepines resemble traditional benzodiazepines, such as diazepam and alprazolam, but differ with the addition of new elements or functional groups. NPS benzodiazepines are often prepared in powder or tablet form and can be mixed with street level drugs, including traditional benzodiazepines and opioids. NPS benzodiazepines are of public health and safety concern due to high potency at low doses producing strong sedation and amnesia. Additional adverse effects include loss of coordination, drowsiness, dizziness, blurred vision, slurred speech, and, in some cases, death.

Summary: Flualprazolam is a potent benzodiazepine bearing structural resemblance to alprazolam. Flualprazolam was first synthesized and reported in the literature in the 1970s. Pharmacological data show that flualprazolam has greater potency than alprazolam. The human toxicity of flualprazolam has not been extensively studied but recent association with drug user death leads professionals to believe this new benzodiazepine retains the potential to cause widespread harm and is of public health concern. At our laboratory alone, flualprazolam has been confirmed in at least 44 biological specimens associated with postmortem (PM) death investigations and driving under the influence of drugs (DUID) investigations in the United States since June 2019. Flualprazolam was first identified in a case from March 2018, however, the popularity of flualprazolam did not increase until recent months. Based on information from colleagues in California, more than 100 cases positive for flualprazolam have been identified and/or reported.

Demographics (n=44)

Date of Collection:
- Jun. to Oct. 2019

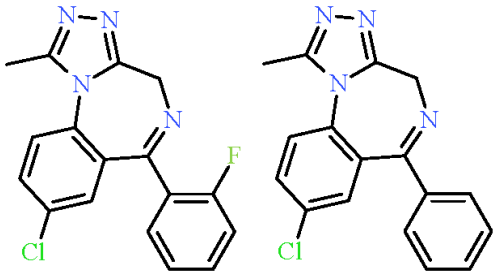
Case Type:
- PM (n=32), DUID (n=12)

Age:
- Avg. 32, Med. 29
- Range: 18 to 67

Sex:
- Male (n=37), Female (n=4)

Concentration (ng/mL):
- Avg. 17, Med. 10
- Range: <2.0 to 88

Other Notable Findings:
- Fentanyl (n=19)
- Etizolam (n=6)



Flualprazolam **Alprazolam**

Recommendations for Clinicians

- Become familiar with the signs and symptoms associated with benzodiazepine use (e.g. sedation, amnesia, drowsiness, etc.).
- Be aware that clinical effects produced by NPS benzodiazepines could differ from those of conventional benzodiazepines.
- NPS benzodiazepines are often sold or ingested in combination with other substances (e.g. opioids). Be mindful that illicit drugs have limited quality control that often impact the expected clinical effects.
- Counsel about the dangers of NPS benzodiazepine products and other drugs.

Recommendations for Laboratories

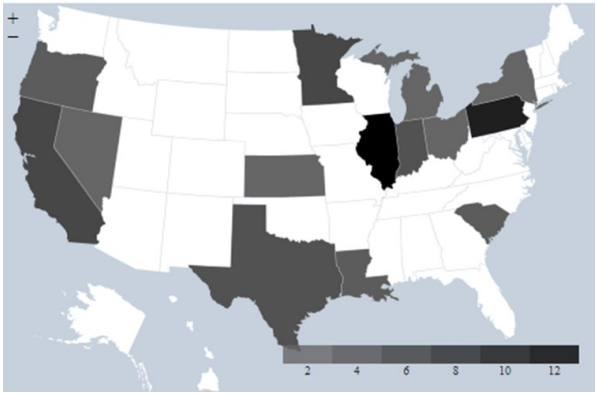
- Utilize analytical data available publicly for the identification of flualprazolam and other NPS if reference standards are not available.
- Utilize previously developed non-targeted testing protocols for NPS benzodiazepines.
- Develop sensitive and up-to-date testing procedures for NPS benzodiazepines. Flualprazolam concentrations are typically less than 20 ng/mL.
- Prioritize analytical testing of seized drug samples taken from drug overdose scenes during death investigations.
- Share data on drug seizures with local health departments, MEs, and coroners.

Recommendations for MEs & Coroners

- Test for new benzodiazepines and their biomarkers in suspected overdose cases.
- Be aware that ELISA screening for NPS benzodiazepines may not be able to detect the newest generation of compounds; consider mass spectrometry-based screening.
- Be aware that concentrations of NPS benzodiazepines in biological specimens can vary. GC-MS sensitivity may not be adequate. Accurate interpretation of findings may be linked to case history.

Recommendations for Public Health

- Implement surveillance for rapid identification of drug overdose outbreaks.
- Study drug use patterns and combinations.
- 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 NPS benzodiazepine use.



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References and Related Articles:

• Hester, JB. (19 October 1976). "Patent US3987052 - 6-Phenyl-4H-s-triazolo[4,3-a][1,4]benzodiazepines." https://patents.google.com/patent/US3987052A/en
• NPS Discovery: Flualprazolam
• WHO: Critical Review Report — Flualprazolam
• NIDA: Benzodiazepines and Opioids

Rapid NPS Testing Now Available:

If your agency suspects opioid and/or benzodiazepine 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@frfoundation.org