

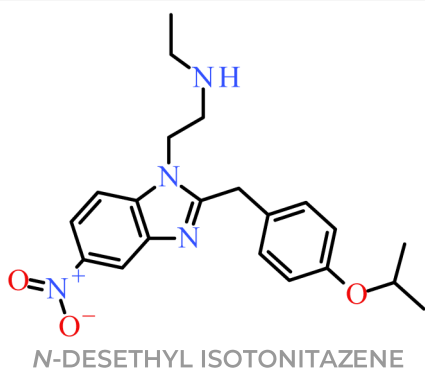
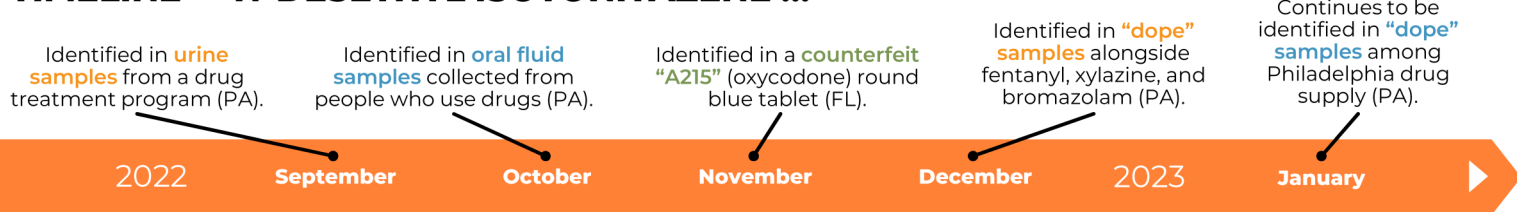
NEW POTENT SYNTHETIC OPIOID—*N*-DESETHYL ISOTONITAZENE— PROLIFERATING AMONG RECREATIONAL DRUG SUPPLY IN USA

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 *N*-desethyl isotonitazene.

BACKGROUND: Synthetic opioids (e.g., fentanyl, fentanyl analogues) are chemically manufactured drugs, often having unknown potency and adverse effects or health risks. Synthetic opioids are frequently mixed with more traditional opioids (e.g., heroin) and other drugs in unregulated drug markets creating additional risk and danger for people who use recreational drugs. Synthetic opioids may be distributed in powder or tablet form. In the United States (USA), an alarming increase in the number of deaths linked to synthetic opioid use has been reported. Primary adverse effects associated with synthetic opioid use are sedation and respiratory depression, leading to death.

SUMMARY: *N*-Desethyl isotonitazene is a new synthetic opioid bearing structural resemblance to **isotonitazene** and recently emergent nitazene analogues. *N*-Desethyl isotonitazene is dissimilar in chemical structure to fentanyl, the synthetic opioid most commonly encountered, but this subclass of new opioids has been proliferating in the wake of the scheduling of fentanyl analogues. *N*-Desethyl isotonitazene is a known metabolite of isotonitazene; however, it has now emerged as a primary drug in its own right. Most nitazene analogues encountered retain opioid receptor activity and potency similar to or greater than fentanyl. *In vitro* **pharmacological data** show that *N*-desethyl isotonitazene is an active opioid agonist and is approximately 20x more potent than fentanyl. In December 2022, *N*-desethyl isotonitazene was first reported by **NPS Discovery** (Florida); however, first identifications were observed as early as September 2022. To date, seven drug material samples (“dope” powders) collected from the Philadelphia drug supply have tested positive for *N*-desethyl isotonitazene. In December 2022, the **Philadelphia Department of Public Health** issued an alert regarding the discovery of this new nitazene analogue in the city’s drug supply. The toxicity of *N*-desethyl isotonitazene has not been examined or reported but recent association with overdoses among people who use drugs leads professionals to believe this synthetic opioid has the potential to cause harm and is of high public health concern.

TIMELINE — *N*-DESETHYL ISOTONITAZENE ...



“DOPE” SAMPLES CONTAINING *N*-DESETHYL ISOTONITAZENE

LOCATION: Philadelphia, PA, USA

NUMBER OF SAMPLES: 7+

CONTENTS (PURITY RANGE):

- ▶ Xylazine (49% to 76%)
- ▶ Fentanyl (1.1% to 5.1%)
- ▶ *N*-Desethyl Isotonitazene (0.05% to 0.4%)
- ▶ Bromazolam (trace to 2.5%)
- ▶ Flubromazepam (trace)
- ▶ *para*-Fluorofentanyl (trace)



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 other drugs onboard or precipitation of withdrawal, which may be more severe with faster onset.
- Be mindful that drugs have limited quality control, containing undeclared substances that impact clinical effects or findings.
- Counsel about the harms and dangers of synthetic opioid products and other drugs.

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.
- Raise awareness about the risks, harms, and dangers associated with opioid use.
- Make naloxone available to people who use drugs. Notify personnel that naloxone remains effective at reversing opioid overdoses caused by nitazene analogues.
- Be aware that fentanyl test strips are not effective at detecting nitazene analogues.

RECOMMENDATIONS FOR LABORATORIES

- Utilize analytical data available publicly for the identification of *N*-desethyl isotonitazene if a reference standard is not immediately available.
- Utilize previously developed non-targeted testing protocols or develop sensitive and up-to-date testing procedures for synthetic opioids and novel drugs.
- Prioritize analytical testing of drug materials obtained from drug overdose scenes during death investigations.
- Share data on synthetic opioid drug seizures with local health departments, medical examiners, coroners, and related communities.

RECOMMENDATIONS FOR MEDICAL EXAMINERS & CORONERS

- Test for new synthetic opioids and their biomarkers (if known) in suspected opioid overdose cases.
- Be aware that ELISA screening for synthetic opioids is not specific or specialized for the newest generations of drugs — Mass spectrometry-based screening is necessary.
- Be aware that concentrations of synthetic opioids in biological specimens can vary and GC-MS sensitivity may not be adequate.
- Consult with forensic toxicologists about novel opioid activity, potency, and association with overdose and/or death.

