

Synthetic Stimulant Market Rapidly Changing as *N,N*-Dimethylpentylone Replaces Eutylone in Drug Supply Typically Sold as “Ecstasy” or “Molly”



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 stimulant *N,N*-dimethylpentylone.

Background: Synthetic stimulants are chemically manufactured drugs with sub-classifications based on their structural relation to amphetamine or cathinone. Synthetic stimulants, including substituted cathinone analogues (e.g., eutylone), can retain both stimulant and hallucinogenic properties, and can cause associated health risks. Synthetic stimulants are often prepared and distributed in powder, capsule, or tablet form, and may be sold as “Ecstasy”, “Molly”, or “MDMA” (3,4-methylenedioxymethamphetamine) on recreational drug markets. In the United States (U.S.), synthetic stimulants have been associated with adverse effects and linked to cardiac effects resulting in death. Adverse effects can include hyperthermia, dehydration, arrhythmias, hallucinations, and serotonin syndrome.

Summary: In 2020 and 2021, the substituted cathinone **eutylone** was the most commonly encountered synthetic stimulant to appear in forensic casework, despite the drug being considered federally scheduled as an isomer of pentylone since March 2017 according to the U.S. Drug Enforcement Administration (DEA). In September 2021, eutylone was recommended for international control. It is this notice that likely created a shift in the NPS drug market, which would later be noted by declining eutylone positivity and increasing *N,N*-dimethylpentylone positivity. *N,N*-Dimethylpentylone was first identified in toxicology samples in the U.S. in Q3 2021, marking the initial insurgence of this drug into the supply and the beginning of its proliferation. To date, *N,N*-dimethylpentylone has been identified in 32 toxicology cases, including antemortem and postmortem investigations, in addition to drug material cases. *N,N*-Dimethylpentylone is not explicitly scheduled in the U.S.; however, it could be considered an isomer of *N*-ethyl pentylone (Schedule I). Of note, pentylone is a metabolite of *N,N*-dimethylpentylone.

Case Breakdown

Case Type:

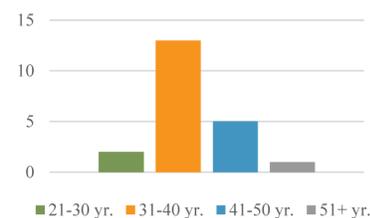
- Postmortem (n=26)
- DUID (n=1)
- Unknown (n=5)

Date of Collection:

- August 2021 to March 2022

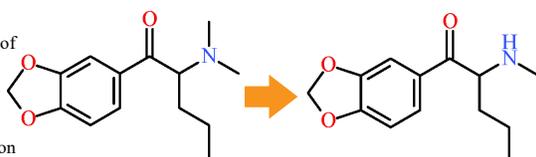
Other Notable Findings:

- Pentylone (n=23)
- Eutylone (n=5)
- Methamphetamine (n=11)
- Fentanyl / Opioids (n=13)
- No Other Drugs (n=8)

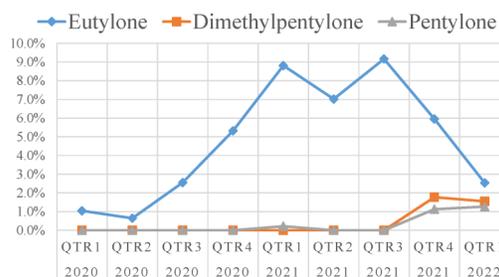


Recommendations for Public Health

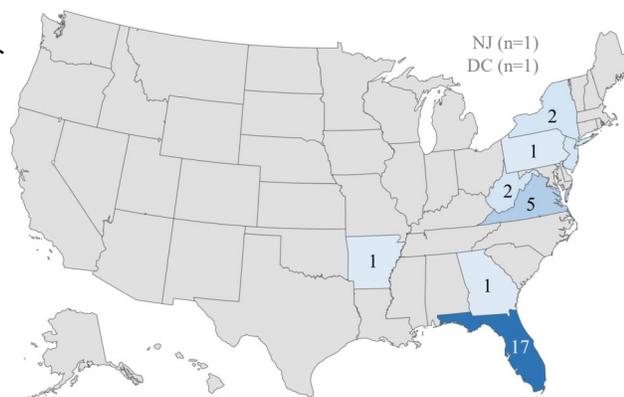
- Implement surveillance for rapid identification of drug use and overdose outbreaks.
- Engage local poison centers and clinicians to assist with treatment of affected patients.
- Track and monitor geographical drug distribution and trends.
- Track demographics and known risk factors for people who use stimulant/hallucinogen drugs.
- Raise awareness about the risks and dangers associated with synthetic stimulant use.



N,N-Dimethylpentylone → Pentylone



Geographical Distribution of *N,N*-Dimethylpentylone in the U.S.



Recommendations for Laboratories

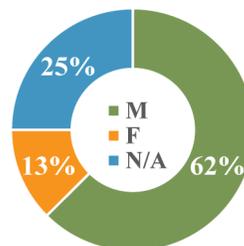
- Utilize analytical data available publicly for the identification of *N,N*-dimethylpentylone.
- Utilize non-targeted testing protocols or develop sensitive and up-to-date testing procedures.
- Prioritize testing of drug material samples.
- Share data on synthetic stimulant identifications with local health departments, forensic scientists, and related communities.

Recommendations for Clinicians

- Become familiar with the signs and symptoms of synthetic stimulant use (e.g., agitation, hallucinations, excitement, elevated pulse, arrhythmias, serotonin syndrome).
- Be mindful that recreational drugs have limited quality control, containing undeclared substances that impact expected clinical effects or findings.
- Counsel about the potential harms of “Ecstasy”, “Molly”, and “MDMA” products and use.

Recommendations for MEs & Coroners

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



Conc. in Postmortem Blood [ng/mL] (n=5)

	<i>N,N</i> -Dimethylpentylone	Pentylone
Mean (±S.D.)	270 ± 400	120 ± 170
Median	87	37
Range	33 - 970	10 - 420

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References and Related Articles:

- Koppe, H.; Ludwig, G.; and Zeile, K. (1964) *Aryl-alpha-Aminoketone Derivatives*. CH Boehringer Sohn AG and Co KG, Boehringer Ingelheim GmbH, Assignee. Patent GB1085135A.
- World Health Organization. (2021) *Critical Review Report: Eutylone*. Expert Committee on Drug Dependence 44th Meeting.
- Krotulski et al. (2021) *Eutylone Intoxications—An Emerging Synthetic Stimulant in Forensic Investigations*. *Journal of Analytical Toxicology*, 45 (1), 8-20.

Rapid NPS Testing Now Available:

If your agency suspects synthetic stimulant 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 (CFSRE); a non-profit organization in collaboration with local and federal agencies which can provide rapid testing after novel drug outbreaks in the United States.

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