

Bromazolam – the Most Frequently Identified NPS Benzodiazepine in 2023

NPS Discovery Webinar – Friday July 7, 2023

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NMS Labs







Introduction

Designer Benzodiazepines

- DBZDs, Novel Benzos, non-FDA Benzos
- EMCDDA monitoring over 33 different DBZDs
- 80% of these detected for 1st time between 2014-2020
 - Etizolam and Flualprazolam placed under international control November 2020
 - Bromazolam emerged & proliferated in replacement due to scheduling efforts
- Novel benzos
 - May be licitly prescribed in certain countries, illicitly supplied to others (NOT bromazolam)
 - Dark web or surface web sales
 - Counterfeit pharmaceuticals
 - Mixed in illicit drug supply
 - "Benzo-dope"



Counterfeit Xanax® tablets containing Flualprazolam.

Source: Papsun DM, Krotulski AJ, Homan J, et al. Flualprazolam blood concentrations in 197 forensic investigation cases. Journal of Analytical Toxicology. 2020. 1-7



Isotonitazene and Flualprazolam white powder. Source: Dr. Alex J Krotulski, CFSRE

Modifications to FDA-Benzodiazepines

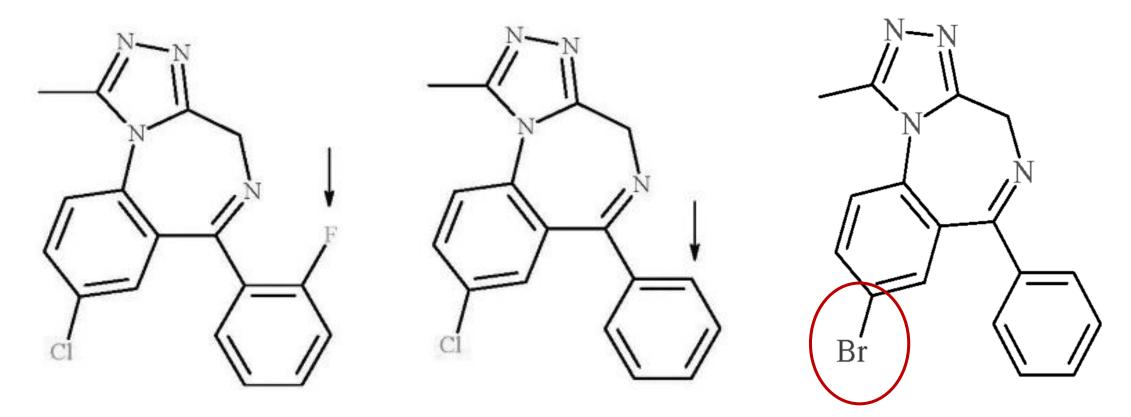


Figure 1. Structure of flualprazolam (left) and alprazolam (right).

Cfsre

Source: Papsun DM, Krotulski AJ, Homan J, et al. Flualprazolam blood concentrations in 197 forensic investigation cases. Journal of Analytical Toxicology. 2020. 1-7

Bromazolam

New Benzodiazepines in Europe – a Review: EMCDDA

FIGURE 2

Timeline of benzodiazepines formally notified to the EU Early Warning System for the first time, 2007–2020



Source: New Benzodiazepines in Europe – a Review. European Centre for Drugs and Drugs Addiction. 2021 Luxembourg. Publications Office of the EMCDDA.

New NPS Benzodiazepines Reported Since 2018

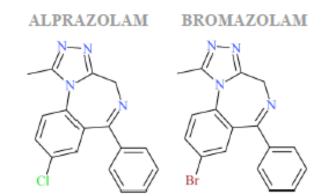


*Only 6 months

June 2022

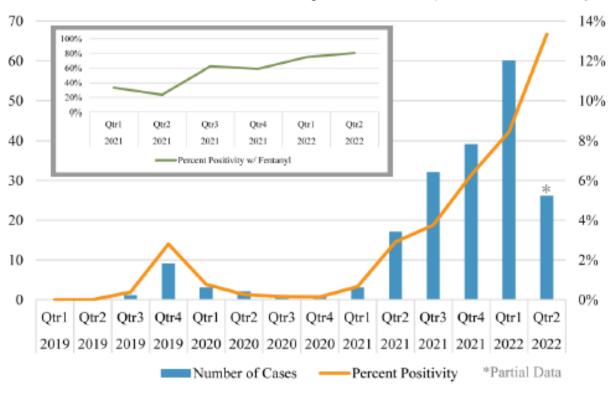
Bromazolam Prevalence Surging Across the United States Driven In Part by Increasing Detections Alongside Fentanyl





Bromazolam Geographical Distribution in the U.S. (Source: NMS Labs, Feb. 2021 to May 2022)

Bromazolam Cases and Positivity in the U.S. (Source: CFSRE)



Public-Alert_Bromazolam_NPS-Discovery_061522.pdf (cfsre.org)



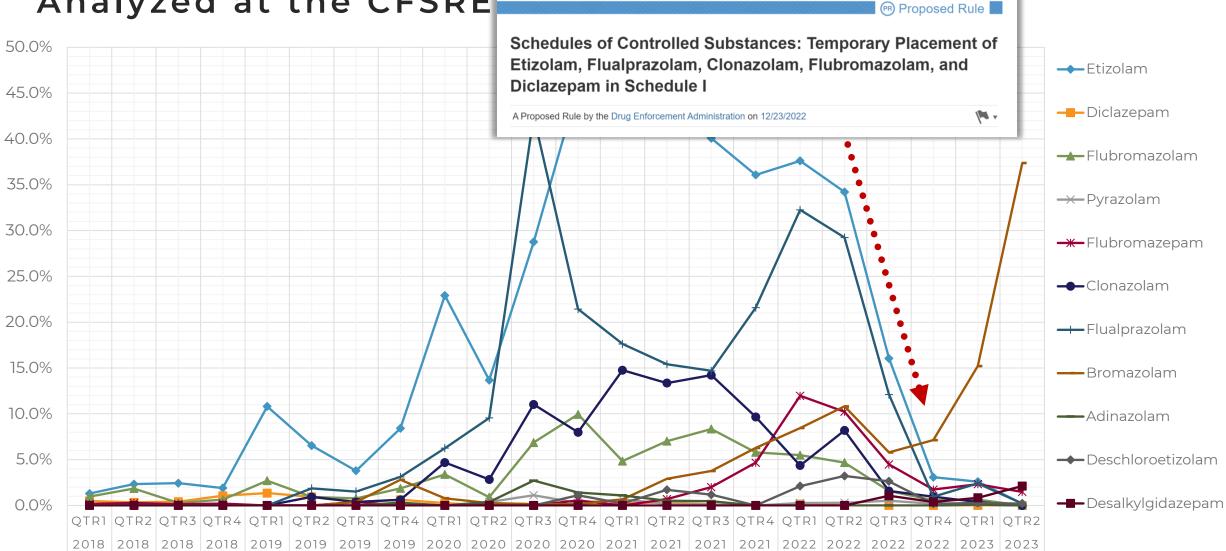


NPS Benzodiazepines

2018	2019	2020	2021	2022	2023*
📘 Etizolam (52%)	Etizolam (54%)	🔲 Etizolam (44%)	🔲 Etizolam (48%)	Etizolam (35%)	Bromazolam (73%)
🔲 Flubromazolam (29%)	📘 Flualprazolam (14%)	🔲 Flualprazolam (33%)	📘 Flualprazolam (20%)	Flualprazolam (29%)	Flubromazepam (7%)
Diclazepam (12%)	Flubromazolam (12%)	Clonazolam (10%)	Clonazolam (15%)	Bromazolam (12%)	Etizolam (6%)
🔲 Flubromazepam (5%)	🔲 Bromazolam (9%)	Flubromazolam (8%)	Flubromazolam (8%)	Flubromazepam (11%)	🔲 Flualprazolam (6%)
Pyrazolam (1%)	🔲 Diclazepam (5%)	🔲 Adinazolam (2%)	🔲 Bromazolam (4%) 🤅	Clonazolam (5%)	🔲 Desalkylgidazepam (4%)
🔲 Flualprazolam (1%)	Clonazolam (4%)	Pyrazolam (1%)	Flubromazepam (2%)	Flubromazolam (5%)	🔲 Flubromazolam (2%)
	Flubromazepam (1%)	Deschloroetizolam (1%)	🔲 Adinazolam (1%)	Deschloroetizolam (3%)	Clonazolam (1%)
	Adinazolam (1%)	—	Deschloroetizolam (1%)	—	Deschloroetizolam (1%)
	—				—

% = of class, *Only 6 months

NPS Benzodiazepine Po Analyzed at the CFSRE



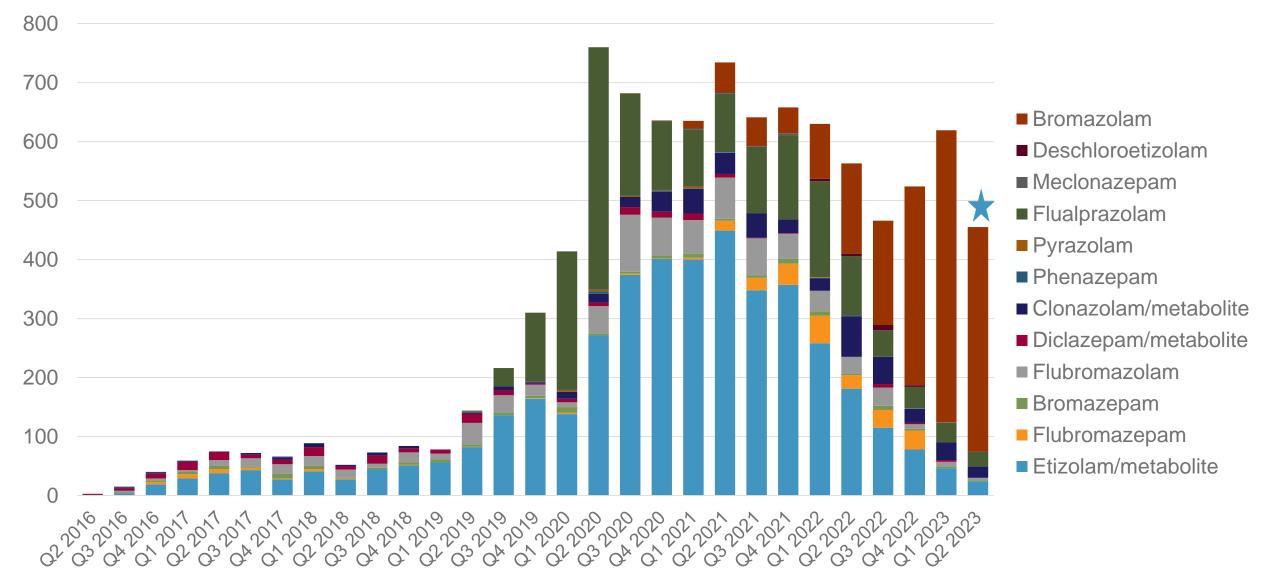
FEDERAL REGISTER

The Daily Journal of the United States Government

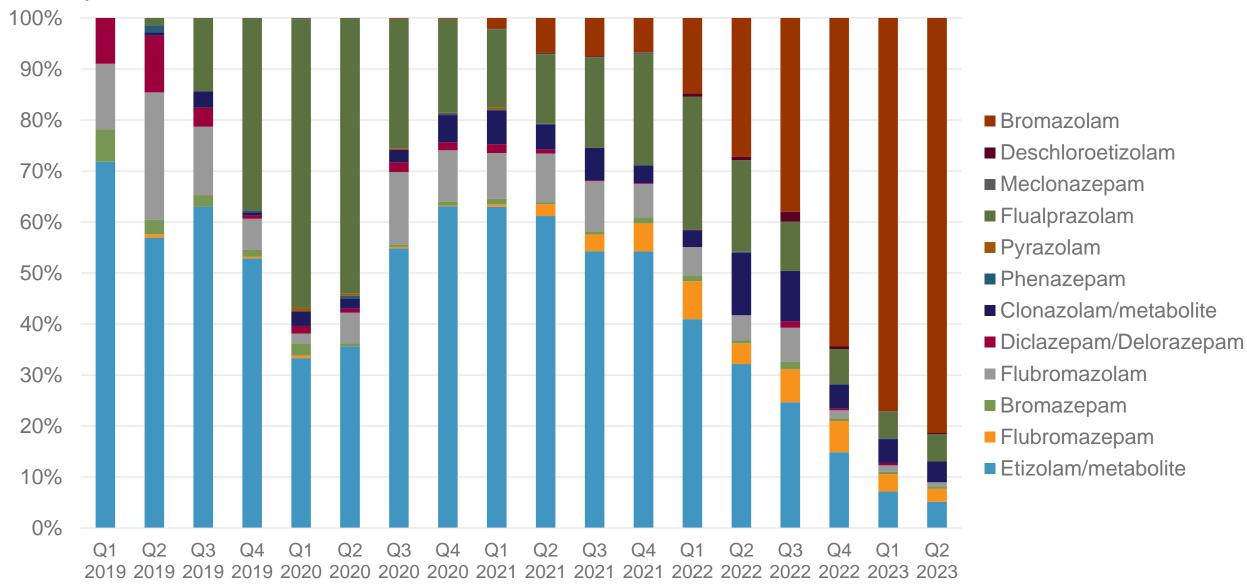
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Reported DBZD in Blood 2016-Q2 2023 – NMS Labs



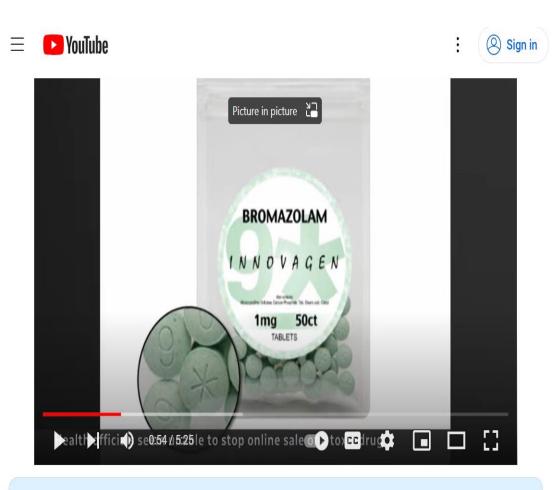
Reported DBZD in Blood 2019- Q2 2023 – Stacked Column



Bromazolam

Reported Findings

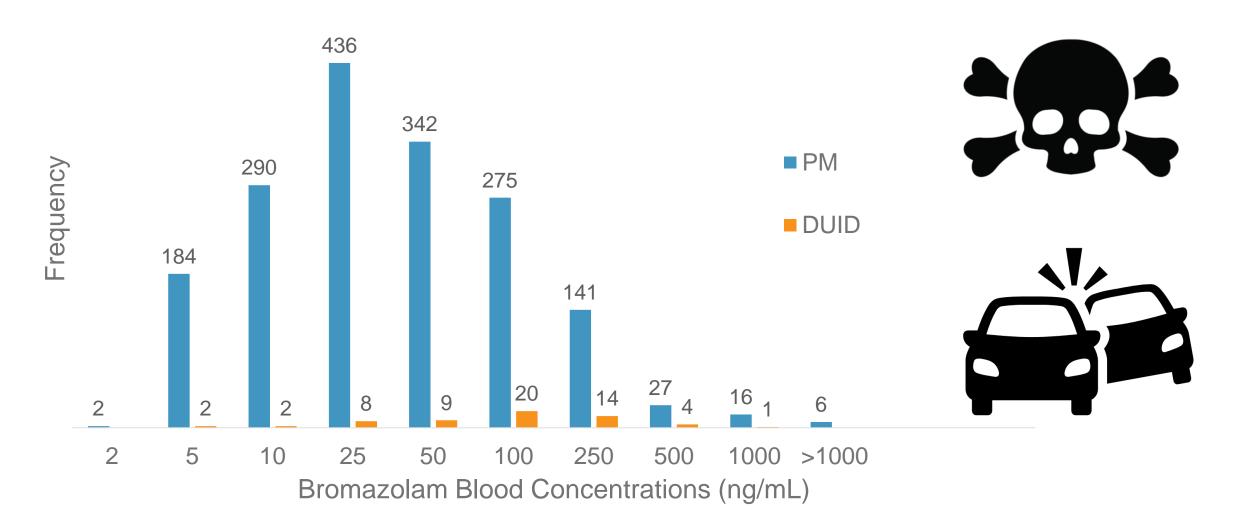
- First reported by NPS Discovery in May 2020
- First toxicology cases reported by NMS Labs were from samples collected in September 2020
- Through end of Q2 2023, total of 1791 blood samples reported for bromazolam (5 qualitatively)
- Postmortem Bloods (n=1719)
- Identified from MEs/coroners, PM test codes, and/or sample source
- Average & Median: 61 ± 236 ng/mL; 23 ng/mL
- Range: 2-5900 ng/mL
- Impaired Driving (n=60)
- Average & Median: 109 ± 144 ng/mL; 67 ng/mL
- Range: 4.3-990 ng/mL



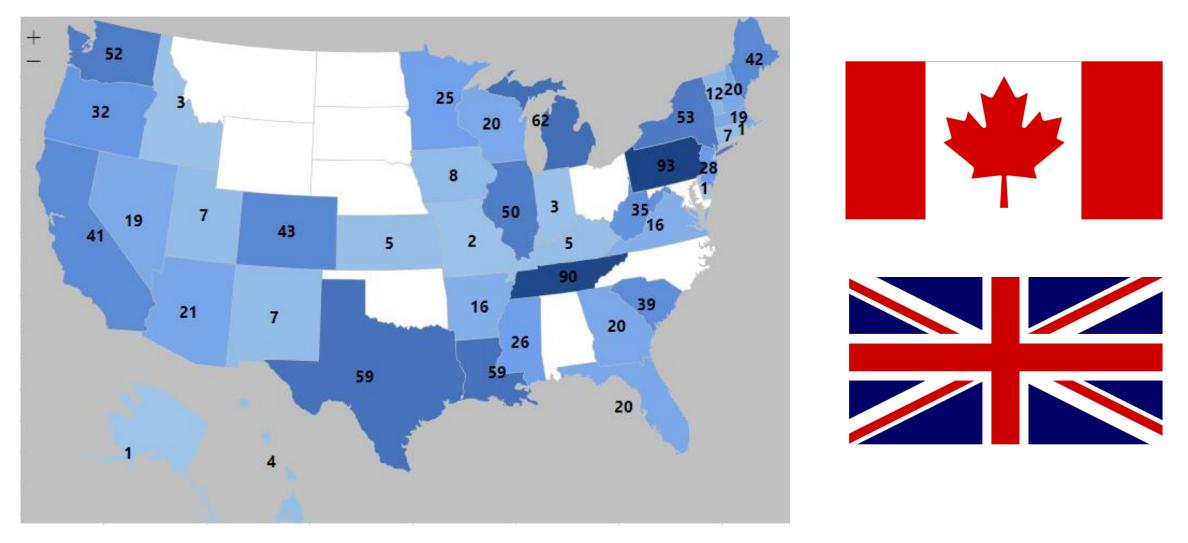
CBC/Radio-Canada is a Canadian public broadcast service. Wikipedia 🖸

Deadly drug just 'a click away,' warns grieving Ontario family

Bromazolam Blood Concentrations – NMS Labs through June 2023



Bromazolam Reported in Blood 2021-June 2023: US States



• Results reported from samples submitted to NMS Laboratories and in which bromazolam testing was added and confirmed positive.



19 19 👩 <u>r/researchchemicals</u> · Posted by u/definitely_a_user 2 days ago

Bromazolam Experience Report

Picked up a 5mg/ml solution of Bromazolam. Couldn't find many solid experience reports so I decided to throw mine out there. For background, I have experience with benzos but I don't take a lot and hadnt had any for around 3 months before this so my tolerance is very low.

I did some quick mafs and came to the conclusion that 4 drops would be around 1mg. Completely unverifiable and slightly bartarded move, but from the few experience reports I found that math lines up.

5:33 4 drops taken, tastes mildly like 1,3-BDO (GHB prodrug) did

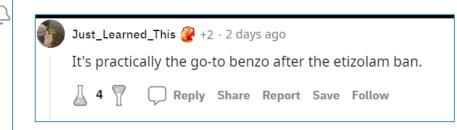
6:17 euphoria and sleepiness have been growing the past hour or so. Time's moving a lot faster than normal.

6:21 my balance is a tiny bit off, as is my hand eye coordination

6:33 smokin weed

8:27 very relaxing night so far

8:42 definitely some amnesic effects from this one but at this dose it's not unbearable. I can still remember stuff but nowhere near as easily. 3 hours in and I still feel some mild euphoria.



alpacasb4llamas · 1 day ago

 \bigcirc

What happened to etiz?? I just picked up a gram of powder easy

🛽 1 🦷 💭 Reply Share Report Save Follow

Just_Learned_This 餐 +2 · 1 day ago

It was banned in a few of the countries that used to supply it. India being the one of note, I believe. I too can find etiz easy but sources aren't as plentiful as they were in 2020.

2 Reply Share Report Save Follow

Case Examples

Postmortem Cases

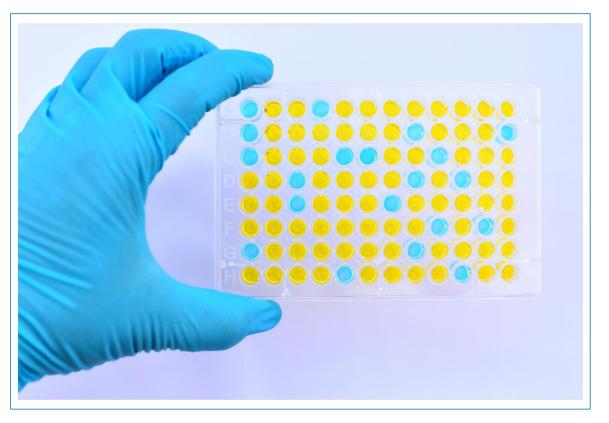
- Case 1: 31 y/o M
- Case History: known heavy alcohol use and drug use, possible drugs (Benzo's) through overseas ordering
- Toxicology Central Blood
 - Ethanol 222 mg/dL
 - Caffeine
 - Delta-9 THC 0.92 ng/mL
 - Bromazolam 1800 ng/mL
- Case 2: 22 y/o F
- Case History: Suspected polysubstance intoxication, autopsy findings included pulmonary edema and cerebral edema
- Toxicology Blood
 - Caffeine, Cotinine, Nicotine, Naloxone
 - Alprazolam 5.1 ng/mL
 - Benzoylecgonine 120 ng/mL
 - Methadone 85 ng/mL
 - Buprenorphine 2.2 ng/mL
 - Norbuprenorphine 1.4 ng/mL
 - Bromazolam 1400 ng/mL

DUID Cases

- Case 1: 33 y/o M
- Case History: Traffic crash in which defendant hit parked car, causing car to roll over. Refused SFSTs or DRE evaluation. Movements were characterized as lethargic, and speech was slow and thick.
- Toxicology:
 - Amphetamine 130 ng/mL
 - Bupropion 22 ng/mL
 - Hydroxybupropion 210 ng/mL
 - Bromazolam 160 ng/mL
- Case 2: 57 y/o M
- Case History: Individual was observed falling asleep while eating breakfast at a restaurant. Vehicle was stopped after failing to stop at a stop sign and following too close to another vehicle. Delayed response to traffic stop. Slurred speech and glassy eyes were noted. Poor performance in SFSTSs (unsteadiness, uncoordinated, etc)
- Toxicology:
 - Bromazolam 990 ng/mL

Toxicology Testing for DBZD

- Many laboratories perform quick and costeffective screening using immunoassay
- DBZD can trigger positive benzodiazepine immunoassay screens due to crossreactivity
- Most routine benzodiazepine confirmations do NOT include DBZD
- Pay attention to unconfirmed benzodiazepine immunoassay screens
- Time of Flight (TOF) screening protocols helpful in data-mining for new compounds, like bromazolam (be wary of bromazolam metabolite alpha-hydroxybromazolam triggering Flubromazolam in TOF)



Summary

- Bromazolam replaced etizolam as predominant designer benzodiazepine, likely in response to global scheduling efforts
 - Likely to stay that way (for now)
 - Critical Review Report by WHO Expert Committee on Drug Dependence October 2022
- Bromazolam seem often with fentanyl
 - In 1051 bromazolam bloods reported between Jan-June 2023, fentanyl positive ~83%
 - "Benzo-dope" street formulations, however, also could be due to prevalence
- Likely underreported (potentially significantly)
 - Variable testing protocols
 - Other findings in cases, so may not seek further testing
- Still a threat to public health & public safety
 - Mixed in illicit drug supply
 - Can exacerbate CNS depression with combo opioids/benzos

Acknowledgements

- CFSRE
 - Alex Krotulski, PhD
 - Sara Walton, MS
- NPS Strategy Team at NMS Labs
- NMS Lab staff
- Jolene Bierly, MSFS, D-ABFT-FT

References

😨 r/researchchemicals · Posted by u/[deleted] 1 year ago

Bromazolam is the benzo I've been searching for all my life

64 upvotes 136 comments 0 awards



💿 r/researchchemicals · Posted by u/the_mega_monster 3 months ago

Bromazolam is ducking potent

24 upvotes 40 comments 0 awards

- Mastrovito R, Trail C, Lina M, et al. (2022) Determination of Cross-Reactivity of Novel Psychoactive Substances with Drug Screen Immunoassays Kits in Whole Blood. Journal of Analytical Toxicology. 46: 726-731
- Mérette SAM, Thériault S, Piramide LEC, et al. (2023) Bromazolam blood concentrations in postmortem cases – a British Columbia perspective. Journal of Analytical Toxicology. 47; 385-392
- Papsun DM, Lamb ME, Chan-Hosokawa A, et al. (2023) Increasing prevalence of designer benzodiazepines in impaired driving: a 5 year analysis from 2017-2021. Journal of Analytical Toxicology. 1-12. epub ahead of print



Thank you! Questions?

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