Recommended Scope for NPS Testing in the United States

NPS SCOPE | Q1 2025

PURPOSE: The objective of this report is to provide updated guidance in developing an appropriate analytical scope of testing for novel psychoactive substances (NPS) in the United States (and around the world) based on current trends and intelligence. *This report is based on information available in Q4 2024 and early Q1 2025 and is subject to change along with the drug market.*

SUMMARY: The NPS landscape is changing rapidly, requiring laboratories to constantly remain abreast of new and emerging drugs locally, nationally, and internationally. To meet individualized needs, laboratories amend existing methods or develop new ones for detection and confirmation of NPS. This can be challenging for scientists as information about NPS detections can be regionalized and/or out-of-date, making it difficult to determine which drugs should be prioritized at a given time. **CFSRE**'s **NPS Discovery** and the **SOFT NPS Committee** have established the below recommendations for NPS scope based on information from extensive collaborations, partnerships, and initiatives which yield national and international perspectives. Suggested cut-off concentrations or reporting limits (in ng/mL) are listed for each NPS. These values are categorized (i.e., <1, 1-10, and >10 ng/mL) and determined based on currently available quantitative data and/or comparison to structurally similar NPS within the given sub-class.

BENZODIAZEPINES		OPIOIDS		STIMULANTS & HALLUCINOGENS		SYNTHETIC CANNABINOIDS		SEMI-SYNTHETIC CANNABINOIDS		MISCELLANEOUS	
TIER ONE (STRONGLY RECOMMEND)											
Bromazolam	1-10	Protonitazene	<1	2F-2oxo-PCE / Fluorexetamine	>10	MDMB-4en-PINACA	<1	Δ^8-THC	1-10	Xylazine	1-10
Desalkylgidazepam†	1-10	Metonitazene	<1	*N,N*-Dimethylpentylone	>10	5F-MDMB-PINACA (5F-ADB)	<1	Δ^8-THC-COOH	1-10	Medetomidine	1-10
Flubromazepam	1-10	Carfentanil	<1	Pentylone	>10	ADB-BINACA (-BUTINACA)	<1	9(R)-HHC / 9(S)-HHC	1-10	Mitragynine	1-10
▪Phenazolam	1-10	*o/m/p*-Fluorofentanyl	1-10	*N*-Isopropyl Butylone	>10	ADB-4en-PINACA	<1	9(R)-HHC-COOH / 9(S)-HHC-COOH	1-10	7OH-Mitragynine	1-10
▪8-Aminoclonazolam‡	1-10	*o/m/p*-Methylfentanyl	1-10	2/3/4-Methylmethcathinone	>10	MDMB-BINACA (-BUTINACA)	<1	-	-	-	-
TIER TWO (RECOMMEND)											
Clonazolam‡	<1	*N*-Pyrrolidino Etonitazene	<1	2/3/4-Chloromethcathinone	>10	5F-MDMB-PICA	<1	Δ^{10}-THC	1-10	Tianeptine	>10
▾Flualprazolam	1-10	*N*-Pyrrolidino Protonitazene	<1	▪alpha-PiHpP / alpha-PHpP	>10	ADB-5'Br-BINACA	<1	Δ^{10}-THC-COOH	1-10	Methorphan	>10
▾Etizolam†	1-10	*N*-Desethyl Isotonitazene	<1	alpha-PiHP / alpha-PHP	>10	MDMB-PICA	<1	THC-O-Acetate	1-10	Etomidate	1-10
Flubromazolam	1-10	*N*-Desethyl Etonitazene	<1	MDPHP / MDPiHP	>10	▪4F-MDMB-BINACA	<1	HHC-O-Acetate	1-10	-	-
TIER THREE (CONSIDER)											
Desalkylflurazepam†	1-10	*N*-Pyrrolidino Metonitazene	<1	2C-B	<1	ADB-5'Br-PINACA	<1	THCP	1-10	BTMPS	1-10
Desalkylquazepam	1-10	▪*N*-Pyrrolidino Isotonitazene	1-10	*N*-Cyclohexyl Methylone	>10	MMB-4en-PINACA	<1	HHCP	1-10	Phenibut	>10
Pyrazolam	1-10	▪*N*-Desethyl Protonitazene	<1	▾Eutylone	>10	4F-MDMB-BICA	<1	CBDP	1-10	-	-
Deschloroetizolam	1-10	*N*-Propionitrile Chlorphine	<1	*N*-Ethyl Pentedrone	>10	▪ADB-CHMINACA	<1	▪HHCH	1-10	-	-

Note: This may not be an all-inclusive list. Laboratories should consider additional NPS for inclusion (or exclusion) based on local, national, and/or international trends.

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Acknowledgements: These scope recommendations were developed by the Society of Forensic Toxicologists (SOFT) NPS Committee in collaboration with the Center for Forensic Science Research and Education (CFSRE) at the Fredric Rieders Family Foundation. This report was prepared by Alex Krotulski, Kayla Ellefsen, Donna Papsun, Elisa Shoff, Svante Vikingsson, Michael Truver, Celia Modell, Lana Goodson, Sandrine Mérette, Amy Patton, Helen Chang, Jillian Neifeld, and Barry Logan. The authors would like to acknowledge scientists and staff at our laboratories for their related involvements and contributions.

Disclaimer: The recommendations in this report are subject to change with time as new information becomes available. †Toxicologists should consider that NPS may appear due to varying pharmaceutical origins.

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PROVIDE FEEDBACK: If you are interested in providing feedback to the SOFT NPS Committee and CFSRE's NPS Discovery program on specific drugs and/or drug classes, the content and formatting of our latest scope recommendations, topics related to NPS and/or NPS testing, or any other items of interest, please email us at npsdiscovery@cfsre.org.

RECOMMENDED NPS METABOLITES: Our recommendations now encompass metabolites of specified NPS to consider in testing scopes, when known or postulated with high certainty based on literature or prior drug similarity. Laboratories should note the following: NPS metabolize to more than one metabolite. Determining the primary metabolite can be difficult and variable based on a variety of factors. NPS metabolites are found at varying abundances in different matrices. This is not intended to be an exhaustive list. Some metabolites listed may be predictive.

RECOMMENDED METABOLITES FOR SPECIFIC NPS				
Bromazolam ▸ alpha-Hydroxy Bromazolam	Protonitazene ▸ *N*-Desethyl Protonitazene & 5-Aminoprotonitazene	2F-2-oxo-PCE ▸ 2F-Deschloronorketamine	MDMB-4en-PINACA ▸ MDMB-4en-PINACA 3,3-Dimethylbutanoic Acid	Δ^8-THC ▸ Δ^8-THC-COOH
Desalkylgidazepam ▸ 3-Hydroxy Desalkylgidazepam	Metonitazene ▸ *N*-Desethyl Metonitazene & 5-Aminometonitazene	*N,N*-Dimethylpentylone ▸ Pentylone	5F-MDMB-PINACA (5F-ADB) ▸ 5F-MDMB-PINACA 3,3-Dimethylbutanoic Acid	9(R)-HHC / 9(S)-HHC ▸ 9(R)-HHC-COOH / 9(S)-HHC-COOH
Flubromazepam ▸ 3-Hydroxy Flubromazepam	*N*-Pyrrolidino Etonitazene ▸ *N*-Pyrrolidino 4'-OH Nitazene	*N*-Isopropyl Butylone ▸ *N*-Desalkyl Butylone	ADB-BINACA (-BUTINACA) ▸ ADB-BINACA *N*-Butanoic Acid & MDMB-BINACA 3,3-Dimethylbutanoic Acid	Δ^{10}-THC ▸ Δ^{10}-THC-COOH
Phenazolam ▸ alpha-Hydroxy Phenazolam	*N*-Pyrrolidino Protonitazene & *N*-Pyrrolidino Isotonitazene ▸ *N*-Pyrrolidino 4'-OH Nitazene	2/3/4-Methylmethcathinone ▸ 2/3/4-Methylcathinone	ADB-4en-PINACA ▸ MDMB-4en-PINACA 3,3-Dimethylbutanoic Acid	Xylazine ▸ 3-Hydroxy Xylazine & 4-Hydroxy Xylazine
Flualprazolam ▸ alpha-Hydroxy Flualprazolam	*N*-Desethyl Isotonitazene ▸ *N,N*-Didesethyl Isotonitazene & 5-Amino *N*-Desethyl Isotonitazene	2/3/4-Chloromethcathinone ▸ 2/3/4-Chlorocathinone	MDMB-BINACA (-BUTINACA) ▸ MDMB-BINACA 3,3-Dimethylbutanoic Acid	Medetomidine ▸ 3-Hydroxy Medetomidine
Clonazolam ▸ 8-Aminoclonazolam	*N*-Desethyl Etonitazene ▸ *N,N*-Didesethyl Etonitazene & 5-Amino *N*-Desethyl Etonitazene	alpha-PiHP / alpha-PHP ▸ beta-Hydroxy-alpha-PiHP / beta-Hydroxy-alpha-PHP	MMB-4en-PINACA ▸ MMB-4en-PINACA 3-Methylbutanoic Acid	Mitragynine ▸ 7-Hydroxy Mitragynine & Pseudoindoxyl Mitragynine
Carfentanil ▸ Norcarfentanil	*o/m/p*-Fluorofentanyl ▸ *o/m/p*-Fluoronorfentanyl	*o/m/p*-Methylfentanyl ▸ *o/m/p*-Methylnorfentanyl	ADB-CHMINACA ▸ MDMB-CHMINACA 3,3-Dimethylbutanoic Acid	(Dextro/Levo) Methorphan ▸ Dextrorphan or Levorphanol

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