Developing an Approach to Standardize the Naming of Novel Psychoactive Substances (NPS)

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Abstract / Overview

Novel psychoactive substances (NPS) continue to appear in forensic casework with increasing regularity as they are mixed with or substituted for traditional drugs or purchased online as legal or alternative “highs”. When NPS are detected by forensic laboratories, their name (and associated identity) is reported on the final forensic report. This information is utilized downstream by various local, state, and federal agencies, including medical examiner and coroner offices certifying deaths and the CDC consolidating information on drug morbidity and mortality. The accurate reporting and tracking of NPS are contingent on the proper use of nomenclature and consistency between laboratories. Mismatches in NPS naming (e.g., *N,N*-dimethylpentylone vs. dipentylone) can cause unnecessary confusion and mistakes in communication, interpretation, and reporting. A central authority on NPS naming is needed; however, the framework for naming must first be established.

NPS nomenclature is complex and not all substances under the NPS classification are necessarily “new”. Some are derived from previous pharmaceutical drug discovery patents but repurposed for illicit use, while others are “old” drugs that have resurfaced and/or are being used in a new or different way. Some drugs are named based on initials of the inventor and numbers based on the series in which they are discovered (e.g., JWH-018 → John W Huffman). Some drugs are named based on abbreviations of their structure features with numbers (e.g., AP-237 → aryl piperazine). Some drugs are given fabricated names that become common language (e.g., fentanyl, etonitazene, alprazolam).

Goals & Workflow

The Center for Forensic Science Research and Education (CFSRE), through its NPS Discovery program and in collaboration with Cayman Chemical, has launched an initiative to help standardize the way NPS are named. The goal is to develop tools and techniques with enhanced workflows to name new and old drugs more accurately and comprehensively. This will facilitate storage and consolidation of information in a database that is easily accessible and searchable, and rapid dissemination of information about the existence of drugs, literature, trends, effects, etc. to the forensic science community.

The primary aim of this initiative is to allow the forensic science community to become more standardized with drug naming and to avoid unnecessary communication issues between forensic laboratories, reporting entities, and other stakeholders (e.g., CDC, DOJ, DEA, etc.).

1. Develop dynamic naming schemes that encompass previously characterized NPS and future drugs.
2. Convene an expert panel to review developed schemes and assist with revisions and iterations.
3. Publish developed naming schemes open-access and disseminate to forensic stakeholders.
4. Implement the use of naming schemes and educate forensic community about their utility.

►►► **New, dynamic naming schemes become primary resources and common practice.**

Synthetic Cannabinoids

Synthetic cannabinoid naming is the most structured under the NPS umbrella, using a semi-systematic alpha-numeric scheme that correlates back to the structure. With the constant emergence of new synthetic cannabinoids, this process needs to be documented yet flexible to include evolving chemistries. Recent examples include: BZO-HEXOXIZID (formerly MDA-19) and CHO-4′Me-5′Br-FUBOXPYRA (formerly CH-FUBBMPDORA).

Semi-Systematic Scheme → [T²] – H – [T³] – T¹CL

H = Head | C = Core | L = Linker | T = Tail | ¹ = Primary Tail Group | ² = Substituted On Tail | ³ = Substituted Within Tail

Examples: ADB-BUTINACA, 5F-MDMB-PICA, MDMB-4en-PINACA

AB-PINACA Formal Name: N-(1-amino-3-methyl-1-oxobutan-2-yl)-1-pentyl-1H-indazole-3-carboxamide

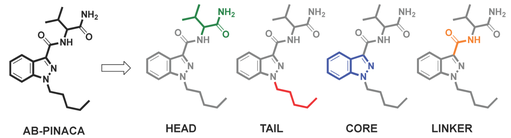


Figure 1: The basic structural components of the synthetic cannabinoid core structure.
H = AB (amino methyl butanoate), C = INA (indazole), L = CA (carboxamide), T = P (pentyl) with no substitutions

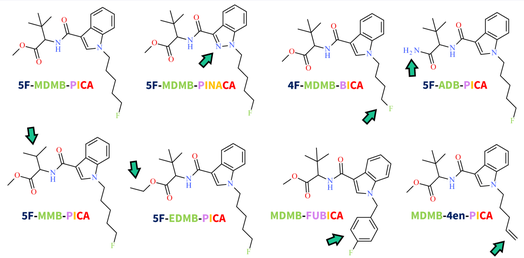


Figure 2: Examples of changes in synthetic cannabinoid names based on head, core, and tail modifications (arrow).

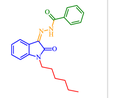
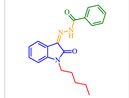
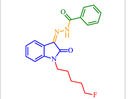
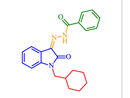
BZO-HEXOXIZID	BZO-POXIZID	5F-BZO-POXIZID	BZO-CHMOXIZID
			
(*Z*)-*N*′-(1-HEXyl-2-OXoIndolin-3-ylidene)BenZOhydraZIDe	(*Z*)-*N*′-(1-Pentyl-2-OXoIndolin-3-ylidene)BenZOhydraZIDe	(*Z*)-*N*′-(1-(5-FluoroPentyl-2-OXoIndolin-3-ylidene) BenZOhydraZIDe	(*Z*)-*N*′-(1-(CycloHexylMethyl)-2-OXoIndolin-3-ylidene) BenZOhydraZIDe
Name: BZO-HEXOXIZID	*Name:* BZO-POXIZID	*Name:* 5F-BZO-POXIZID	*Name:* BZO-CHMOXIZID
Synonyms: **MDA-19, MDA19, MDA 19**	*Synonyms:* **5C-MDA-19, MDA-19 pentyl analogue**	*Synonyms:* **5F-MDA-19, MDA-19 5-fluoropentyl analogue**	*Synonyms:* **CHM-MDA-19, Cyclohexylmethyl MDA-19**

Figure 3: Colored illustration showing how the alpha-numeric components of the formal chemical name are used to derive the semi-systematic names of the new synthetic cannabinoid subclass known as the “OXIZIDs”.

NPS Opioids

NPS opioid naming is primarily based on the drug prototype for the subclass of interest (e.g., fentanyl, etonitazene) which is used as the root term with prefix and suffix modifications to indicate changes in chemical structure. This means the naming scheme for each NPS opioid subclass may be different; however, overall schemes retain some level of semi-systematic nature. One benefit to naming NPS opioids on their prototypical drug is that the name itself often helps indicate the subclass, making its association more evident.

Nitazene Analogues → “Etonitazene” → Eto = ethoxy, nita = nitro, and zene = benzene

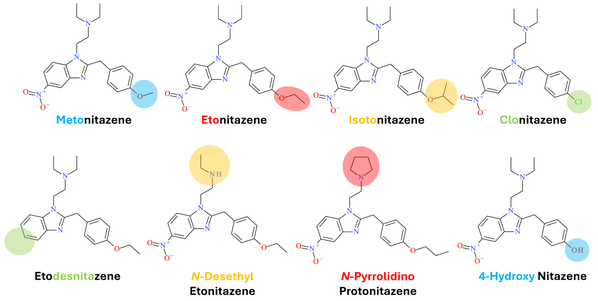


Figure 4: Examples of changes in nitazene analogue names based on structural subcomponent modifications (color).

Fentanyl Analogues

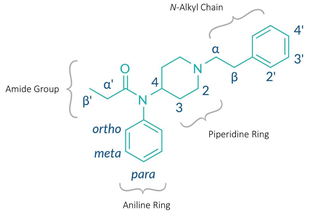


Figure 5: Core structure of fentanyl with primary structural subcomponents showing the manner in which the drug name changes based on the position of modification by using a systematic approach.

[Source: Cayman Chemical]

Naming in Action
Fentanyl
Acetylfentanyl
Valerylfentanyl
Furanylfentanyl
alpha′-Methylfentanyl
para-Fluorofentanyl
3-Methylfentanyl
alpha-Methylfentanyl
beta-Hydroxyfentanyl
4′-Chlorofentanyl
para-Methyl Tetrahydrofuranylfentanyl
para-Fluoro-4′-Fluorofentanyl
Norfentanyl
N-Propionyl Norfentanyl
Benzylfentanyl
Carfentanil

More Information

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Collaborating with NCATS & GSRS

NCATS = National Center for Advancing Translational Sciences
GSRS = Global Substance Registration System

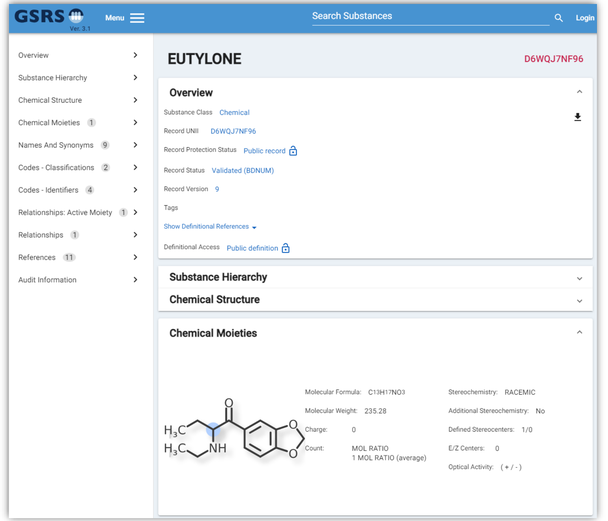

Figure 6: Screen capture of the NPS stimulant eutylone from the GSRS software to show the layout and functionality of the program.

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