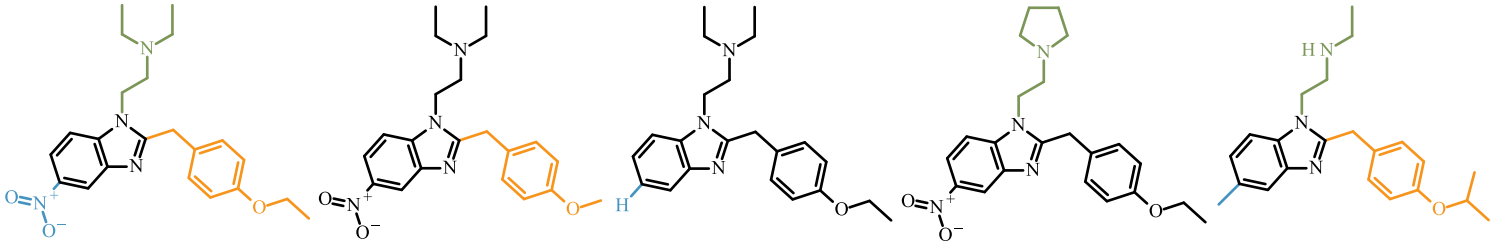
NPS OPIOID NAMING GUIDE

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 based on drug prototype is that the name itself often helps indicate the structural and biological subclass, making association more evident.

NITAZENE ANALOGUES

Nitazene analogue nomenclature stems from the prototypical drug ***Etonitazene***. As such, the name etonitazene was used to develop a semi-structured naming convention to account for modifications to core structural moieties (i.e., benzyl, nitro, and *N,N*-diethylamino groups).

- **Benzyl Group:** Modifications to the benzyl ring are named by adding a prefix in front of the root "nitazene" to reflect the nature of the substituent added.
  - **Examples: Meto**nitazene, **Isoto**nitazene, **Clo**nitazene, **Flu**nitazene, **4-Hydroxy** Nitazene, **Flu**etonitazene, **Methylenedioxy**nitazene, **Ethyleneoxy**nitazene, **Propyl**nitazene
- **Nitro Group:** Nitazene analogues lacking the 5-nitro moiety contain the word "des" prior to the "nitazene" root. Substitutions to the nitro group are then placed in front.
  - **Examples:** Eto**des**nitazene, Meto**des**nitazene, Clo**des**nitazene, **5-Methyl** Eto**des**nitazene
- ***N,N*-Diethylamino Group:** Modifications to the *N,N*-diethylamino moiety are named to reflect that substituent added or removed and the component name is placed in front.
  - **Examples: *N*-Desethyl** Isotonitazene, ***N*-Pyrrolidino** Protonitazene, ***N*-Piperidinyl** Etonitazene, ***N,N*-Dimethylamino** Etonitazene, ***N*-Pyrrolidino** Eto**des**nitazene, ***N*-Pyrrolidino Flu**etonitazene



Etonitazene | ***Meto****nitazene* | *Eto**des**nitazene* | ***N*-Pyrrolidino** *Etonitazene* | ***5-Methyl N*-Desethyl Isoto*des**nitazene***

Figure 1: Structures of nitazene analogues and names based on structural modifications.

FENTANYL ANALOGUES

Fentanyl analogue nomenclature stems from the prototypical drug ***Fentanyl***. As such, the name fentanyl was used to develop a semi-structured naming convention to account for modifications to core structural moieties (i.e., amide, aniline, piperidine, and *N*-alkyl moieties).

- **Amide Group:** Modifications where the amide group differs from that of fentanyl are named by placing the substituent descriptor to the front of the root "fentanyl".
  - **Examples: Acetyl**fentanyl, **Valeryl**fentanyl, **Furanyl**fentanyl, **Isobutyryl**fentanyl
- **Aniline Ring:** Modifications to the aniline ring are generally simple additions where the substituents on the scaffold are noted using *ortho*-, *meta*-, and *para*- (**Figure 2**).
  - **Examples: *ortho*-Methyl**fentanyl, ***meta*-Chloro**fentanyl, ***para*-Fluoro**fentanyl
- **Piperidine Ring:** Modifications to the piperidine ring are generally simple additions where the substituents on the scaffold are noted using 2-, 3-, and 4- (**Figure 2**).
  - **Examples: 2-Fluoro**fentanyl, **3-Methyl**fentanyl, **4-Propionyl** fentanyl
- ***N*-Alkyl Chain:** Modifications to the *N*-alkyl chain can be simple additions or more complex substitutions. Simple additions on the scaffold are noted using 2'-, 3'-, and 4'- (**Figure 2**). Complex substitutions occur when the *N*-phenethyl moiety is removed and as such the root changes to "**nor**fentanyl". The substituent added is then placed in front.
  - **Examples: 4'-Fluoro**fentanyl, ***N*-Propionyl Nor**fentanyl, ***N*-Methyl Nor**fentanyl
  - **Complex Examples: 2'-Fluoro ortho-Fluoro**fentanyl, **ortho-Fluoro Furanyl**fentanyl, ***para*-Chloro Cyclopropyl**fentanyl, ***N*-Methyl *para*-Methyl Phenyl*nor***fentanyl
- *Note: Common (or historical) names exist for some fentanyl analogues which are outside of the scope of this semi-synthetic naming system and remain unchanged.*
  - ***Examples:** Carfentanil, Benzylfentanyl, Remifentanil, Sufentanil, Alfentanil, Ocfentanil*

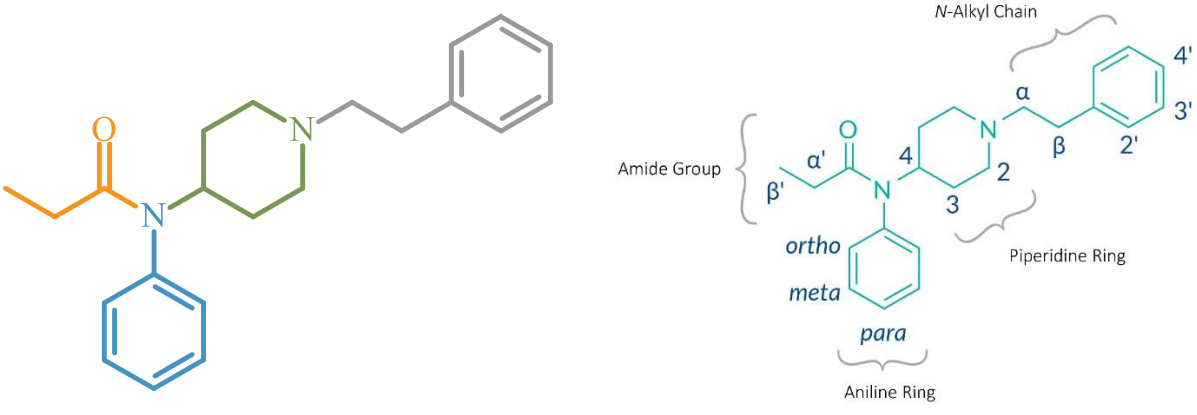


Figure 2: Core structure of fentanyl (left) with primary structural subcomponents showing the manner in which a new drug name changes based on the position of modifications or substitutions by using a semi-systematic approach (right). *[Source: Cayman Chemical]*

About: With funding from the National Institute of Justice (NIJ), the Center for Forensic Science Research and Education (CFSRE) at the Fredric Rieders Family Foundation, in collaboration with Cayman Chemical, is developing and implementing standardized nomenclature and taxonomy in relation to novel psychoactive substance (NPS), with a focus on four main classifications: benzodiazepines, opioids, stimulants and hallucinogens, and synthetic cannabinoids. The goal of this specific initiative is to improve communications regarding NPS and help eliminate confusion by assigning preferred names and naming guides for future NPS.

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