The Naming of Synthetic Cannabinoid Receptor Agonists Explained

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Center for Forensic Science Research & Education

NPS Discovery Webinar Series
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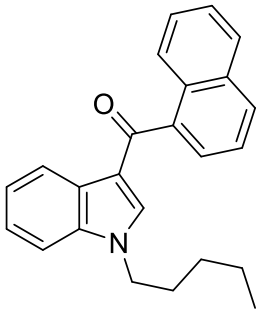
Topics

- Historical naming systems
- Uchiyama Method for naming synthetic cannabinoids
  - Explanation of system
  - Application of system to emerging new structural classes
- Cayman guide for syn cann naming and identification
- Future naming working group

Early synthetic cannabinoid naming



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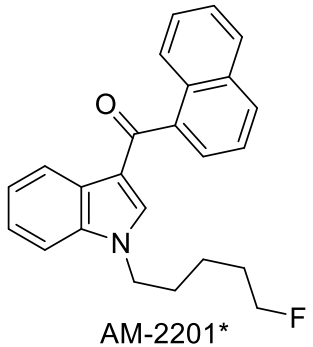

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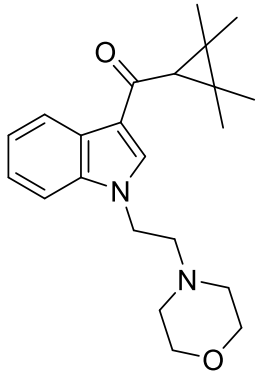

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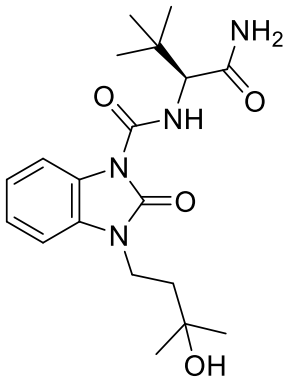

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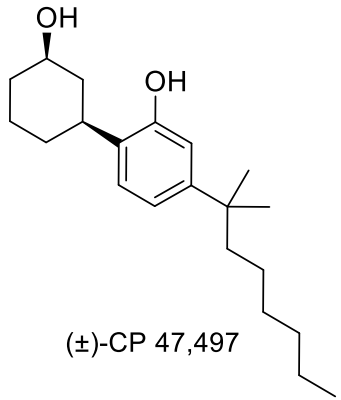
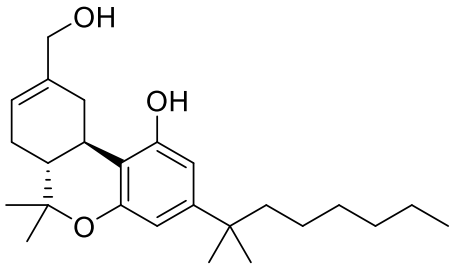


(±)-CP 47,497



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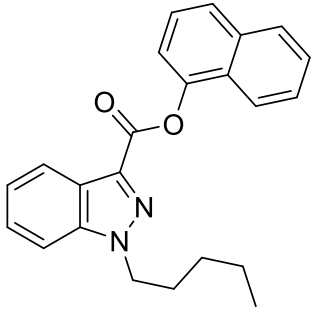

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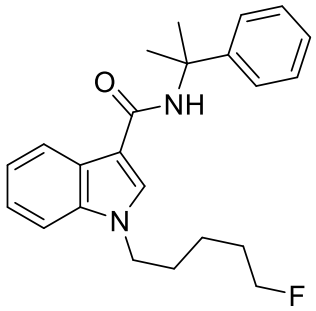
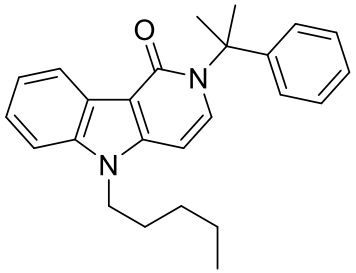


SGT-67

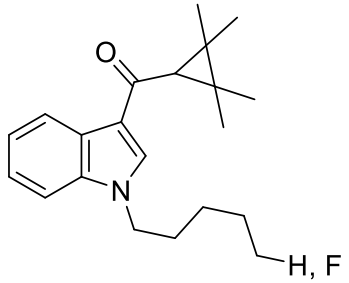


SGT-151

Early cannabinoid researchers

- **A**: Abbott
- **AM**: Alexandros Makriyannis
- **AZ**: AstraZeneca
- **AZD**: AstraZeneca Development
- **Bay**: Bayer AG
- **CE**: Pfizer
- **CP**: Pfizer (CyclohexylPhenols)
- **EA**: Edgewood Arsenal
- **GSK**: GlaxoSmithKline
- **HU**: Hebrew Univ of Jerusalem
- **JHU**: Johns Hopkins University
- **JWH**: John W Huffman
- **KDS**: Kadmus Pharmaceutical Inc.
- **LY**: Eli Lilly
- **RCS**: Research Chemical Suppliers
- **SDB**: Samuel D. Banister
- **SR**: Romano Silvestri
- **UP**: Paolo Urbani
- **X**: Hoffmann-LaRoche

More unusual syn cann naming over time



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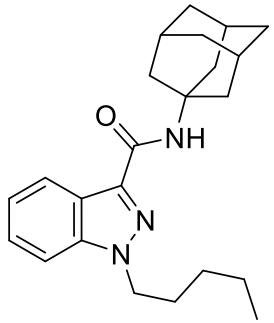
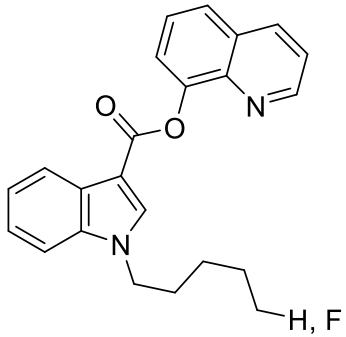
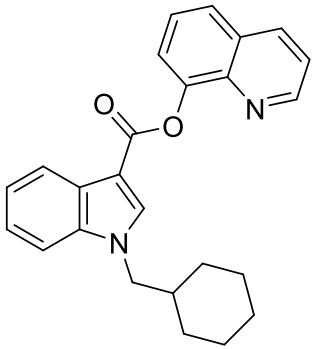
XLR11*



AKB48*



PB-22*
5F-PB-22*



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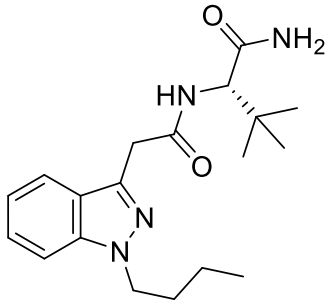
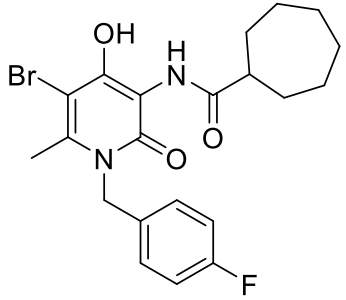
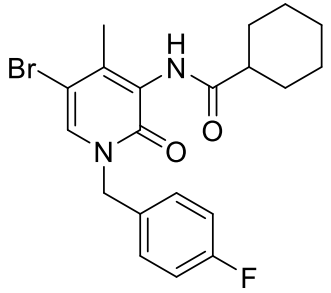


7-ADD
ADB-BUTINAATA



5CP



6TP

Origin of semi-systematic syn cann naming system

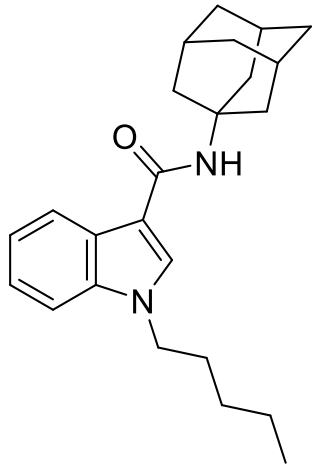
Forensic Toxicol (2012) 30:114–125
DOI 10.1007/s11419-012-0136-7

ORIGINAL ARTICLE

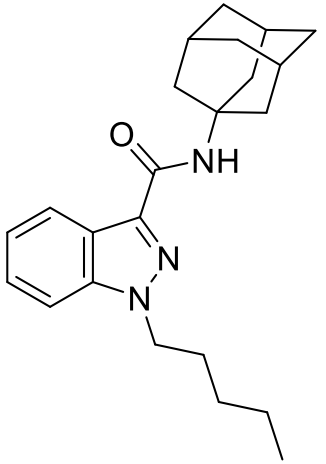
Identification of two new-type synthetic cannabinoids, *N*-(1-adamantyl)-1-pentyl-1*H*-indole-3-carboxamide (APICA) and *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide (APINACA), and detection of five synthetic cannabinoids, AM-1220, AM-2233, AM-1241, CB-13 (CRA-13), and AM-1248, as designer drugs in illegal products

Nahoko Uchiyama · Maiko Kawamura · Ruri Kikura-Hanajiri · Yukihiro Goda

Received: 1 February 2012 / Accepted: 12 March 2012 / Published online: 11 April 2012



APICA
2NE1
SDB-001



APINACA
AKB48

https://link.springer.com/article/10.1007/s11419-012-0136-7

Origin of semi-systematic syn cann naming system

Original Article | Published: 04 November 2012

New cannabimimetic indazole derivatives, *N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-pentyl-1*H*-indazole-3-carboxamide (AB-PINACA) and *N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1*H*-indazole-3-carboxamide (AB-FUBINACA) identified as designer drugs in illegal products

Nahoko Uchiyama, Satoru Matsuda, Daigo Wakana, Ruri Kikura-Hanajiri & Yukihiro Goda

Forensic Toxicology **31**, 93–100 (2013) | Cite this article

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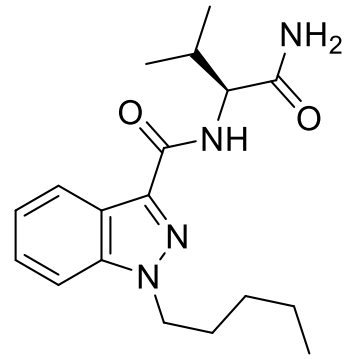
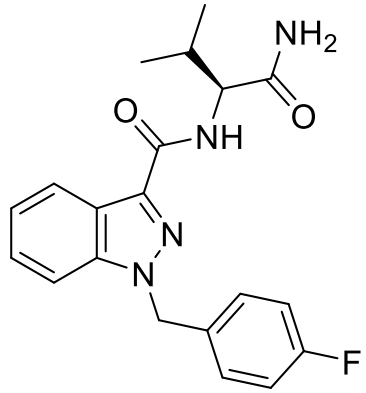


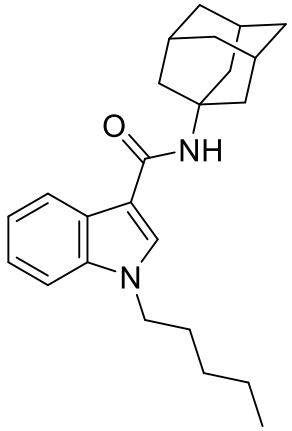
AB-PINACA*



AB-FUBINACA*

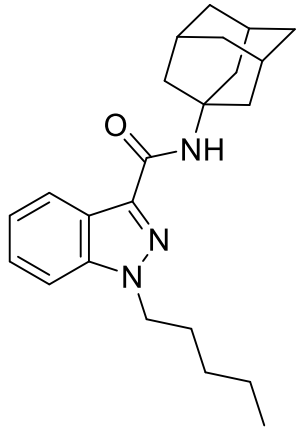
https://link.springer.com/article/10.1007/s11419-012-0171-4

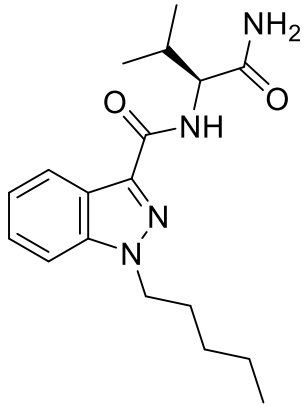
Semi-systematic syn cann naming examples



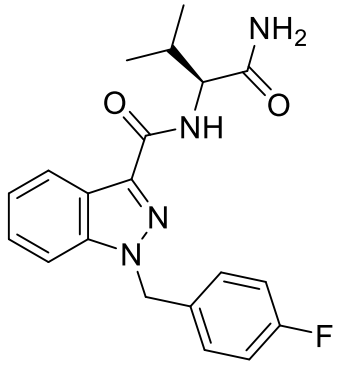
N-(1-**A**damantyl)-1-**P**entyl-1*H*-
Indole-3-**C**arbox**A**mide
(**APICA**)

N-(1-**A**damantyl)-1-**P**entyl-1*H*-
INd**A**zole-3-**C**arbox**A**mide
(**APINACA**)



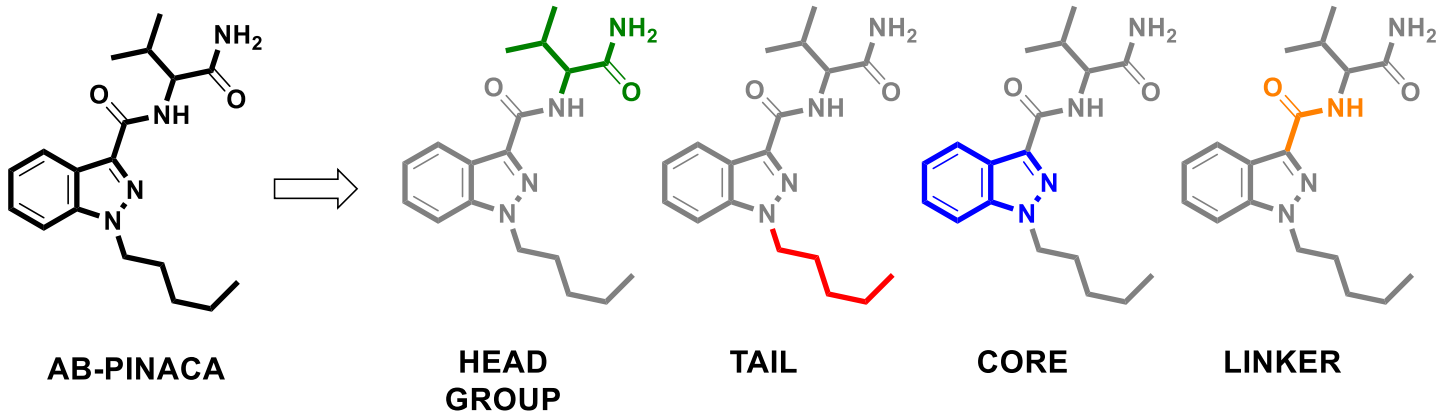


N-(1-**A**mino-3-methyl-1-oxo**B**utan-2-yl)-1-
Pentyl-1*H*-**IN**d**A**zole-3-**C**arbox**A**mide
(**AB-PINACA**)



N-(1-**A**mino-3-methyl-1-oxo**B**utan-2-yl)-1-(4-
Fl**U**oro**B**enzyl)-1*H*-**IN**d**A**zole-3-**C**arbox**A**mide
(**AB-FUBINACA**)

Syn cann naming convention explained



- Molecule divided into four parts
- Use chemical name & each part assigned a letter code
- Letters in code name follows the order:

Head Group - Tail Core Linker

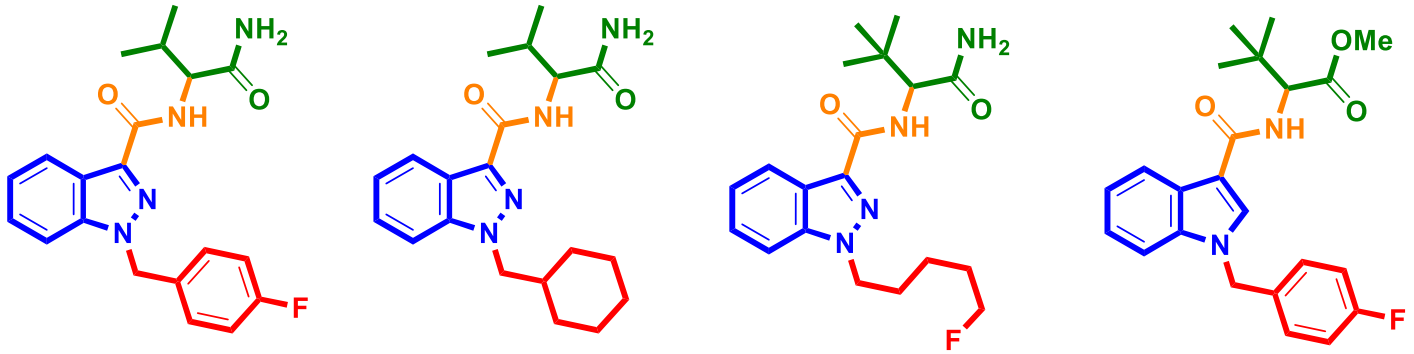
N-(1-**A**mino-3-methyl-1-oxo**B**utan-2-yl)-1-**P**entyl-**IN**d**A**zole-3-**C**arbox**A**mide

AB-PINACA

- http://www.emcdda.europa.eu/topics/pods/synthetic-cannabinoids for division of molecule into parts

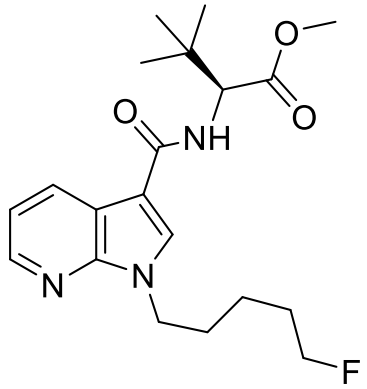
More Uchiyama naming method examples

- **Using the chemical name: Head Group – Tail Core Linker**

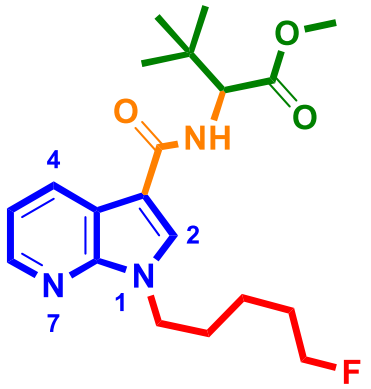


- *N*-(1-**A**mino-3-methyl-1-oxo**B**utan-2-yl)-1-(4-**F**l**U**oro**B**enzyl)-1H-**IN**d**A**zole-3-**C**arbox**A**mide
  AB-FUBINACA
- *N*-(1-**A**mino-3-methyl-1-oxo**B**utan-2-yl)-1-(**C**yclo**H**exyl**M**ethyl)-1H-**IN**d**A**zole-3-**C**arbox**A**mide
  AB-CHMINACA
- *N*-(1-**A**mino-3,3-**D**imethyl-1-oxo**B**utan-2-yl)-1-(**5**-**F**luoro**P**entyl)-1H-**IN**d**A**zole-3-**C**arbox**A**mide
  5F-ADB-PINACA
- **M**ethyl (S)-2-(1-(4-**F**l**U**oro**B**enzyl)-1H-**I**ndole-3-**C**arbox**A**mido)-3,3-**D**i**M**ethyl**B**utanoate
  MDMB-FUBICA

Current scaffolds – substituted indoles



5F-MDMB-P7AICA



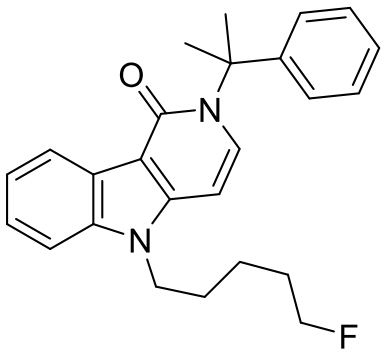
5F-MDMB-P7AICA

- Azaindole used instead of chemical name due to simplicity: "7-**A**za**I**ndole" vs. "1H-pyrrolo[2,3-b]pyridine"

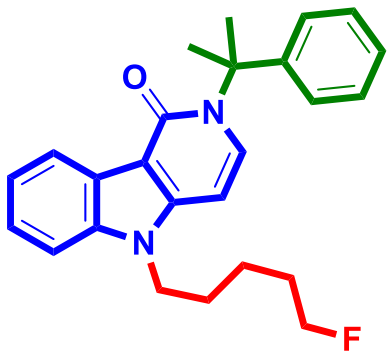
- Number is used to indicate position of aza-nitrogen in the indole ring system: **7A**za**I**ndole

Head-TailCoreLinker

The PeGACLONES



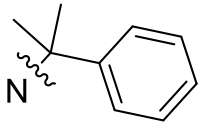
5F-CUMYL-PeGACLONE



5F-CUMYL-PeGACLONE

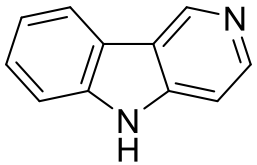
- Use common name for core instead of IUPAC as with azaindoles
- Based on gamma-carbolines

CUMYL =

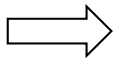


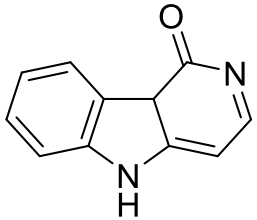
vs

(2-phenylpropan-2-yl)



gamma-carboline





GAmma-**C**arbo**L**in-1-**ONE**

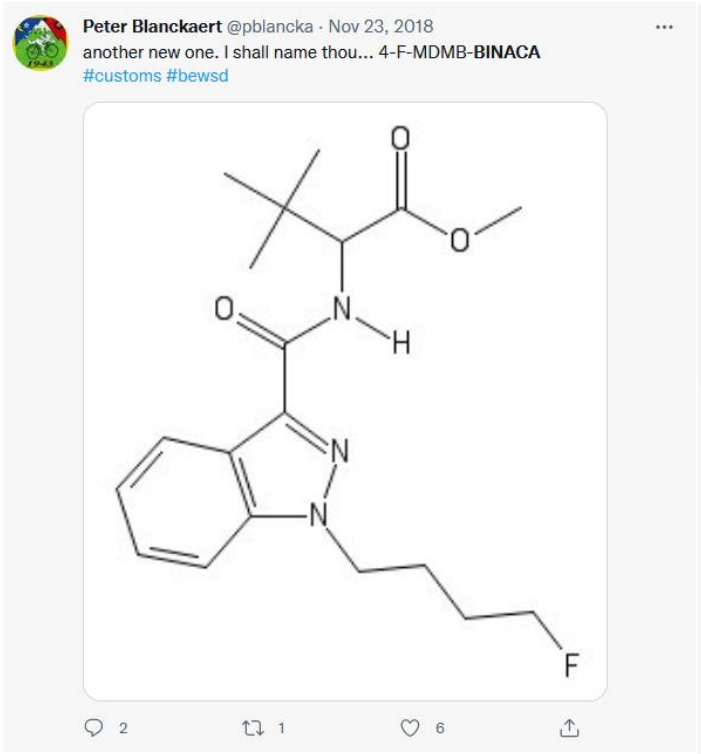
vs:

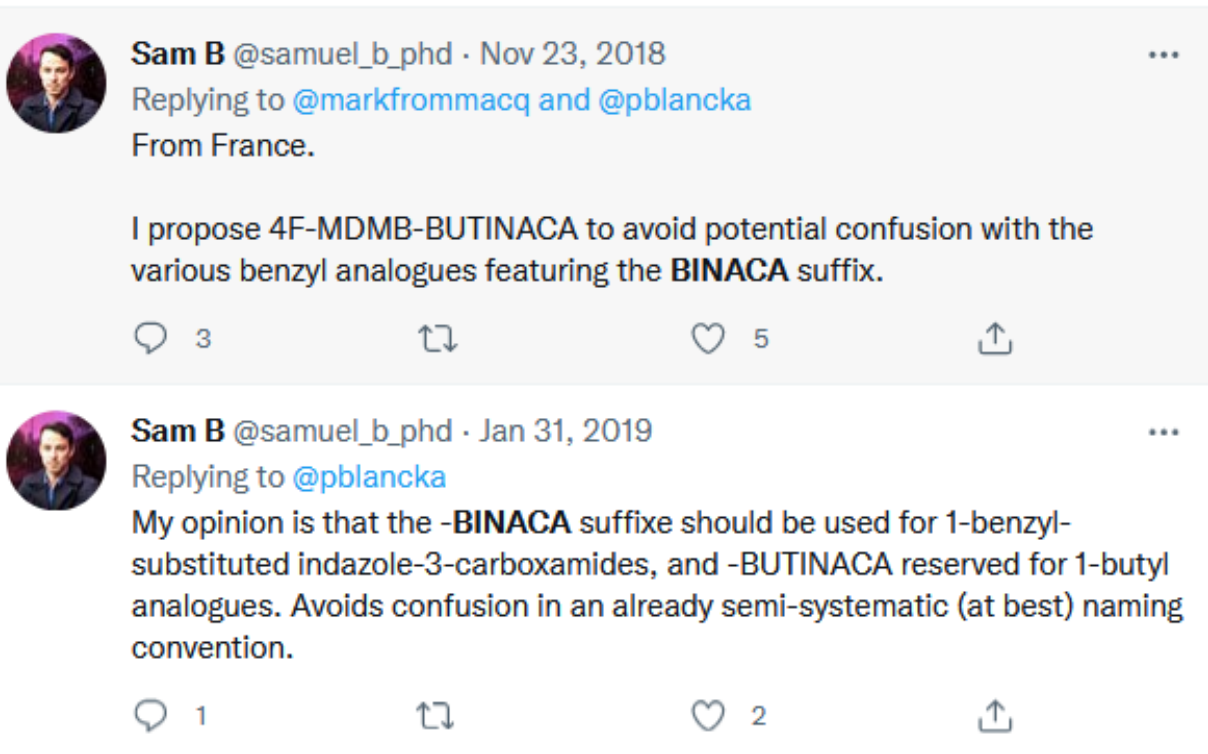
Head-TailCoreLinker

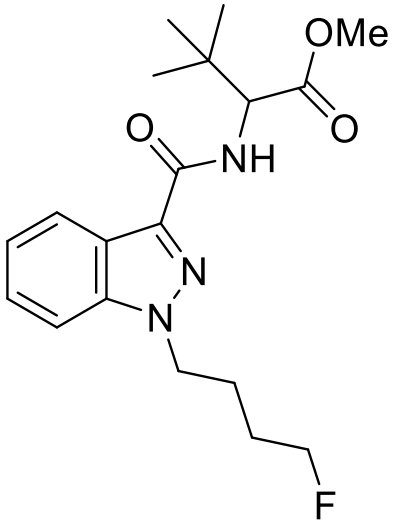
5,9b-dihydro-1H-pyrido[4,3-b]indol-1-one

The use of “BINACA”

- “BINACA” and “BUTINACA” are often used interchangeably when referring to this molecule







4F-MDMB-BUTINACA
4F-MDMB-BINACA
(#26645)

- Cayman suggests using BUTINACA when referencing indazoles with butyl tails

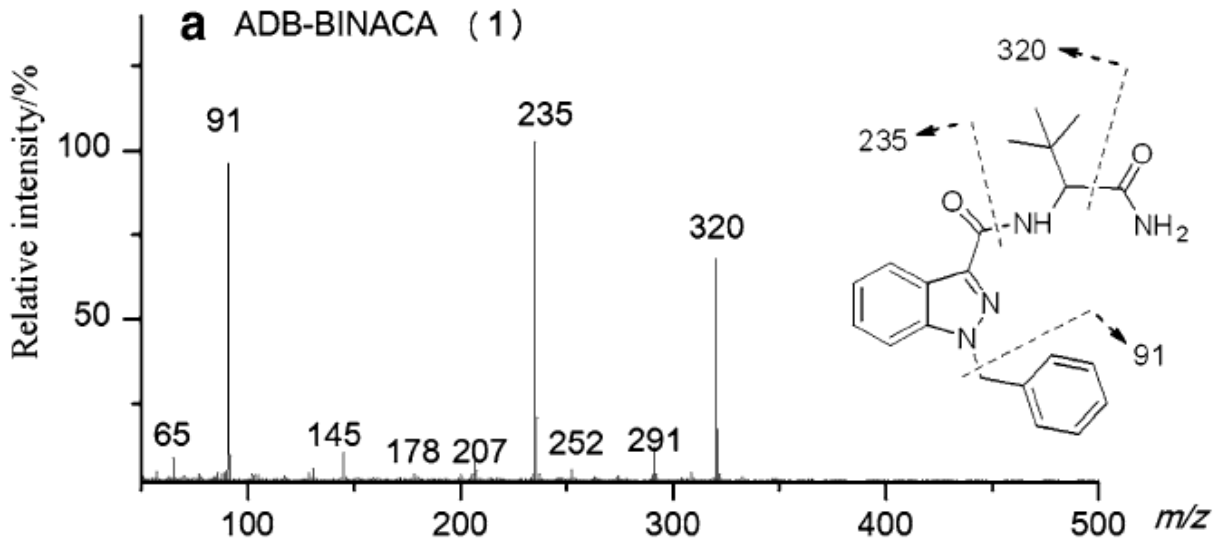
BINACA and BUTINACA are not synonymous

Forensic Toxicol (2016) 34:133–143
DOI 10.1007/s11419-015-0297-2

ORIGINAL ARTICLE

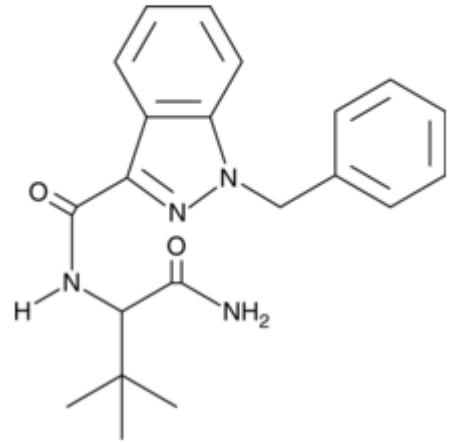
Four types of cannabimimetic indazole and indole derivatives, ADB-BINACA, AB-FUBICA, ADB-FUBICA, and AB-BICA, identified as new psychoactive substances

Zhenhua Qian[1] · Zhendong Hua[1] · Cuimei Liu[1] · Wei Jia[1]



ADB-BINACA

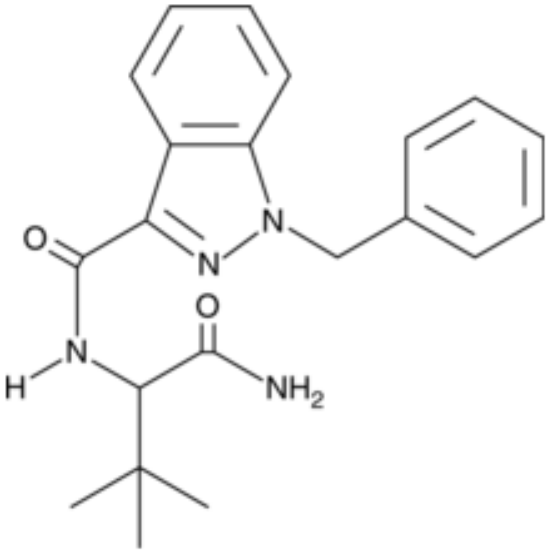
Item No. 18757



BINACA, BUTINACA, & BENZINACA

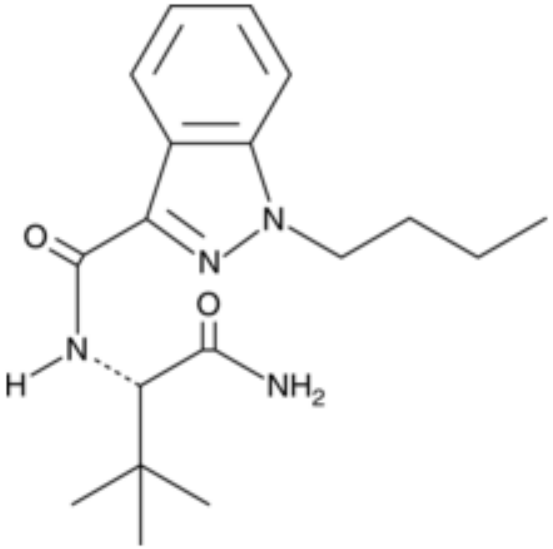
ADB-BINACA

Item No. 18757



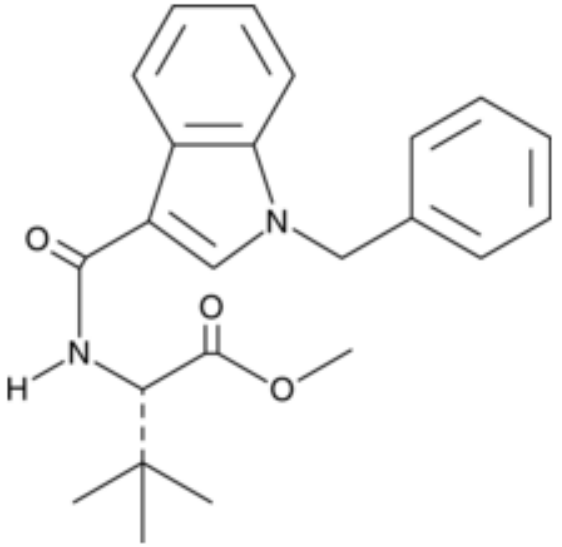
ADB-BUTINACA

Item No. 29350



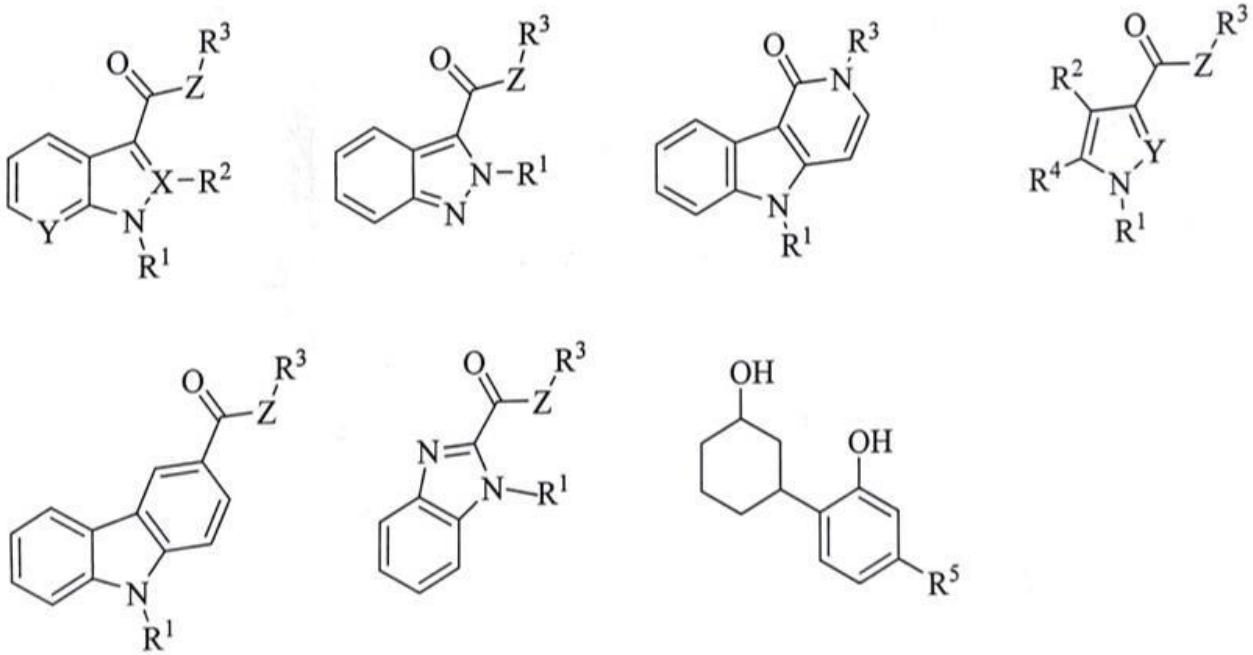
MDMB-BENZICA

Item No. 35135



- Cayman now uses “BENZ” to refer to benzyl tails to avoid any confusion

Synthetic Cannabinoids: China generic class-ban 2021



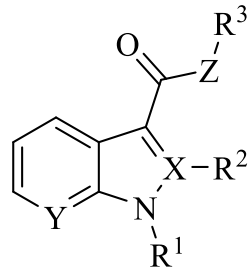
- **X** represents N or C.
- **Y** represents N or CH.
- **Z** represents O or NH or no atom.

PLACE HOLDER FOR ALEX?

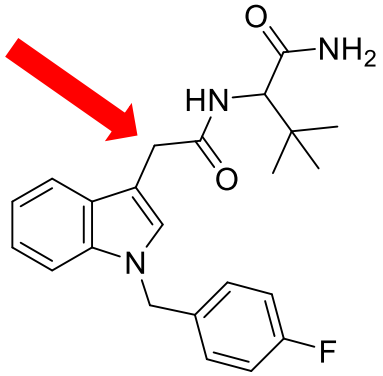
- **R1** represents substituted or unsubstituted C3-C8 hydroxy group; substituted or unsubstituted heterocyclic group containing 1-3 heteroatoms; substituted or unsubstituted methyl or ethyl group substituted by heterocyclic group containing **1-3** heteroatoms.
- **R2** represents hydrogen or methyl or no atom.
- **R3** represents substituted or unsubstituted C6-C10 aryl group; substituted or unsubstituted C3-C10 hydroxy group; substituted or unsubstituted heterocyclic group containing 1-3 heteroatoms; substituted or unsubstituted methyl or ethyl group substituted by heterocyclic group containing 1-3 heteroatoms.
- **R4** represents hydrogen; substituted or unsubstituted phenyl group; substituted or unsubstituted benzyl group.
- **R5** represents substituted or unsubstituted C3-C10 hydroxy group.

https://www.unodc.org/LSS/Announcement/Details/ff032a29-2e14-4dab-b7d8-ab86d355c809

Applying naming system to the newest structures

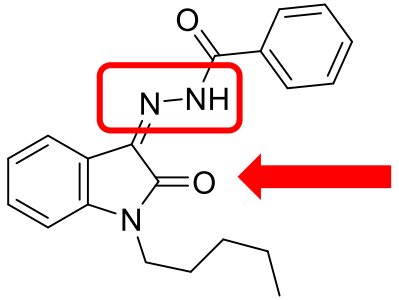


China Generic class-ban



FUB-ACADB

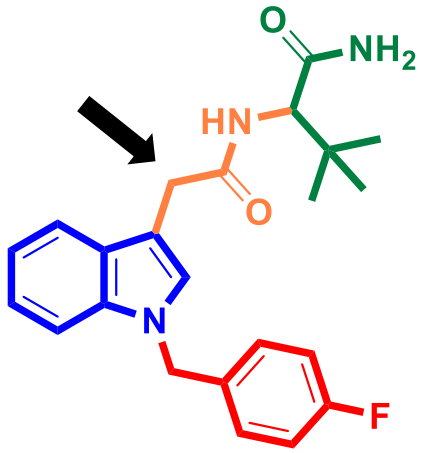
ADB-FUBIATA
“IATAs”



pentyl MDA-19

BZO-POXIZID
“OXIZIDs”

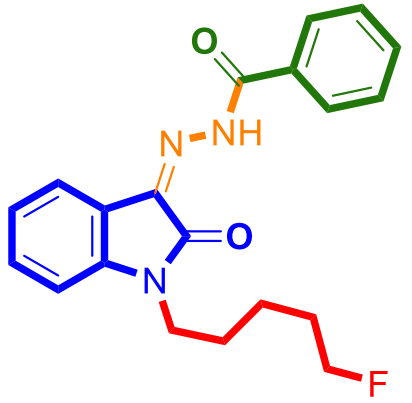
Applying naming system to new structures



2-(2-(1-(4-**F**l**U**oro**B**enzyl)-1H-**I**ndol-3-yl)**A**ce**TA**mido)-3,3-dimethylbutanamide

ADB-FUBIATA

[The letters **ADB** come from an alternate name of the head group: 1-**A**mino-3,3-**D**imethyl-1-oxo**B**utan-2-yl]



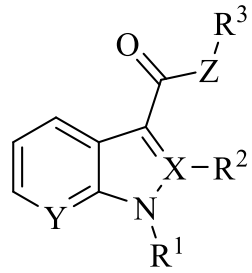
CORE/LINKER combo:
common scaffold = "OXIZID"

N'-(1-(**5-F**luoro**P**entyl)-2-**OX**o**I**ndolin-3-ylidene)**B**en**ZO**hydra**ZID**e

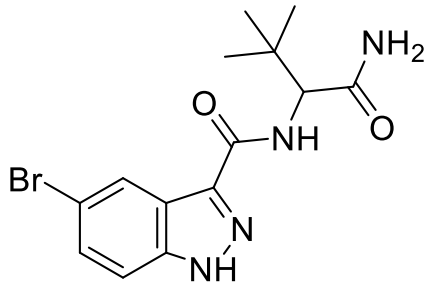
5F-BZO-POXIZID

Head-TailCoreLinker

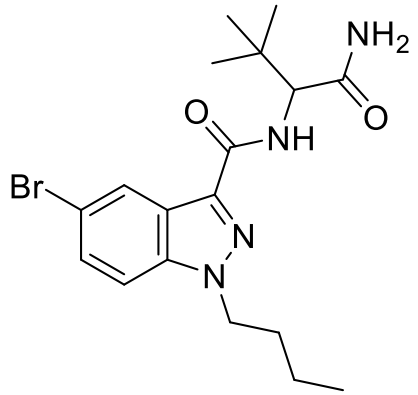
Applying naming system to new structures



China Generic class-ban



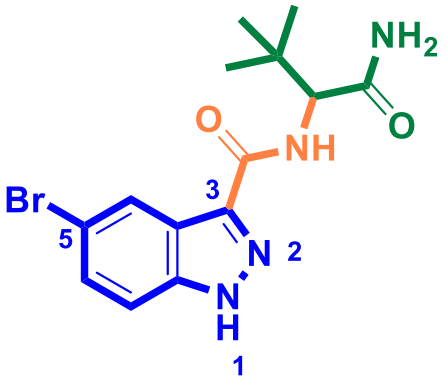
ADB-5Br-INACA



5Br-MMBA(N)-073

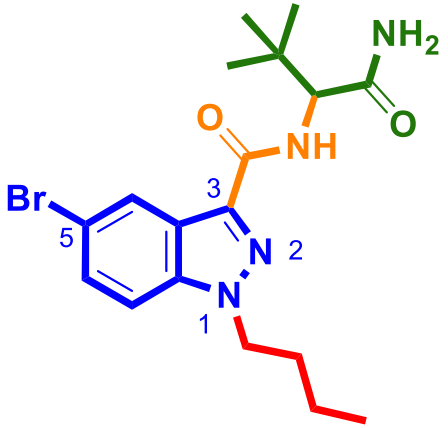
ADB-5’Br-BUTINACA

Applying naming system to new structures



N-(1-**A**mino-3,3-**D**imethyl-1-oxo**B**utan-2-yl)-**5-Br**omo-1*H*-**IN**d**A**zole-3-**C**arbox**A**mide

"ADB-5Br-INACA"

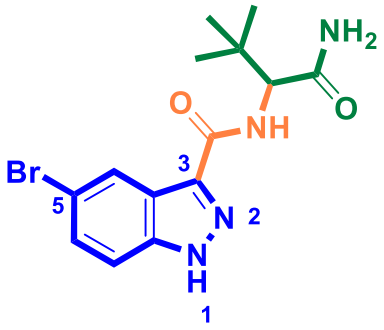


N-(1-**A**mino-3,3-**D**imethyl-1-oxo**B**utan-2-yl)-**5-Br**omo-1-**BUT**yl-1*H*-**IN**d**A**zole-3-**C**arbox**A**mide

ADB-5'Br-BUTINACA

Head-TailCoreLinker

Applying naming system to new structures



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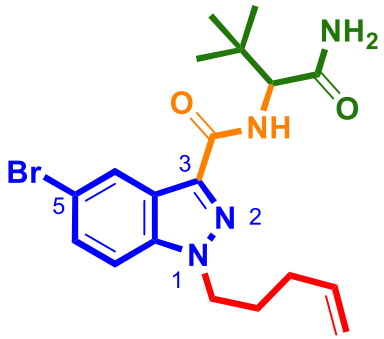
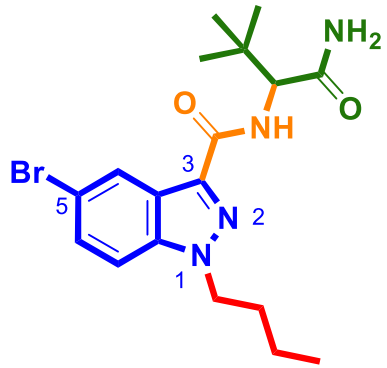
"ADB-5Br-INACA"



N-(1-**A**mino-3,3-**D**imethyl-1-oxo**B**utan-2-yl)-**5-Br**omo-1-(**P**ent-**4-en**-1-yl)-1*H*-**IN**d**A**zole-3-**C**arbox**A**mide

ADB-5Br-4en-PINACA
ADB-4en-P-5Br-INACA

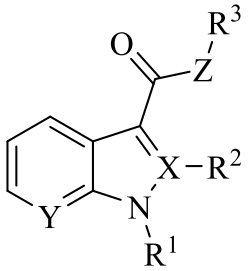


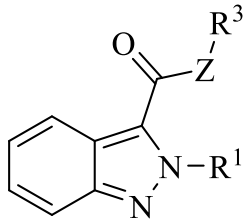
N-(1-**A**mino-3,3-**D**imethyl-1-oxo**B**utan-2-yl)-**5-Br**omo-1-**BUT**yl-1*H*-**IN**d**A**zole-3-**C**arbox**A**mide

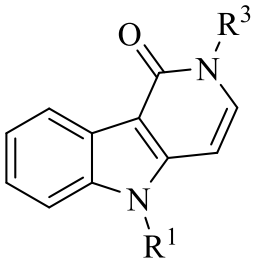
ADB-5'Br-BUTINACA

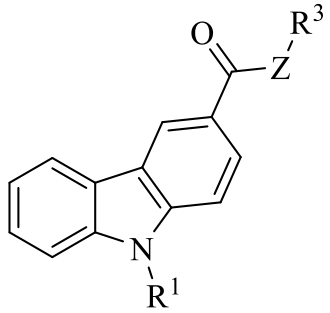
Head-TailCoreLinker

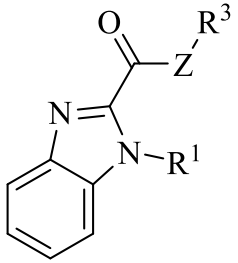
Applying naming system to new structures

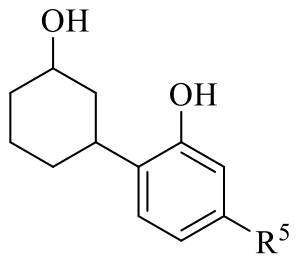


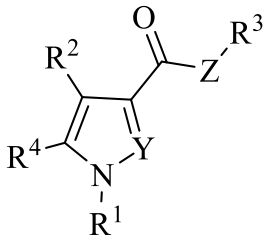


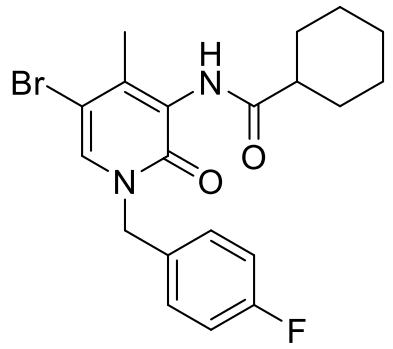








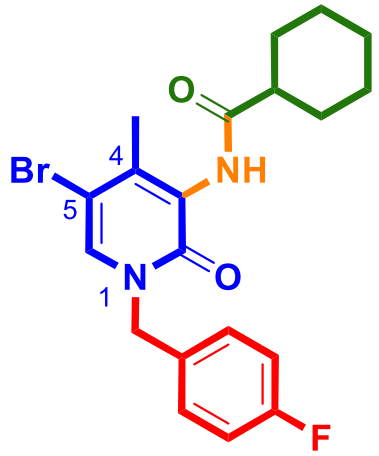




6TP
CH-FUBBMPDORA

- https://aipsin.com/newsubstance/999/
- https://www.policija.si/apps/nfl_response_web/0_Analytical_Reports_final/CH-FUBBMPDORA-ID-3189-22_report.pdf (March 2023)
- European Journal of Medicinal Chemistry 211 (2021) 113116
- NOT covered by China ban

Applying the naming system to more new scaffolds



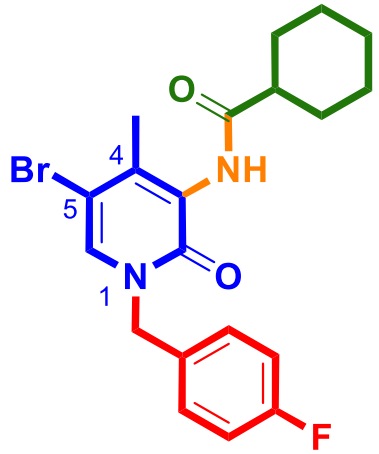
N-(**5-Br**omo-1-(4-**F**I**U**oro**B**enzyl)-**4-Me**thyl-2-**OX**o-1,2-dihydro**PYR**idin-3-yl)**C**yclo**H**exanecarb**O**x**A**mide

CHO-4'Me-5'Br-FUBOXPYRA

2-oxo-pyridines- "OXPYRAs"

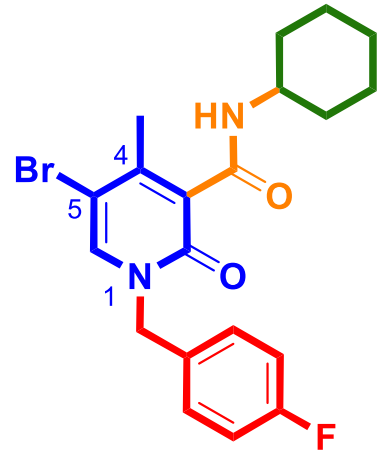
Head-TailCoreLinker

Applying the naming system to more new scaffolds



N-(**5**-**Br**omo-1-(4-**F**l**U**oro**B**enzyl)-**4**-**Me**thyl-2-**OX**o-1,2-dihydro**PYR**idin-3-yl)**C**yclo**H**exanecarb**O**x**A**mide

CHO-4'Me-5'Br-FUBOXPYRA



5-**Br**omo-*N*-**C**yclo**H**exyl-1-(4-**F**l**U**oro**B**enzyl)-**4**-**Me**thyl-2-**OX**o-1,2-dihydro**PYR**idine-3-**C**arbox**A**mide

CH-4'Me-5'Br-FUBOXPYRCA

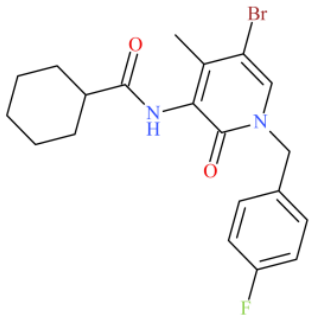
Head-TailCoreLinker

CHO-4'Me-5'Br-FUBOXPYRA

NPS Discovery — New Drug Monograph 2023

cfsre | NPS DISCOVERY | Pinellas County Forensic Laboratories | Cayman Chemical

CHO-4'Me-5'Br-FUBOXPYRA



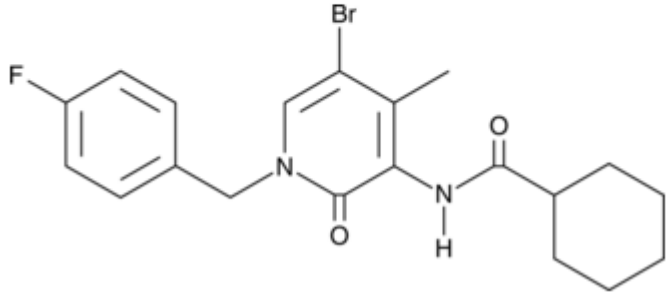
NPS SUBCLASS
Synthetic Cannabinoid
REPORT DATE
June 28, 2023
SAMPLE RECEIVED
March 10, 2023
SAMPLE TYPE
Drug Material

Preferred Name	CHO-4'Me-5'Br-FUBOXPYRA
Synonyms	CH-FUBBMPDORA, 6TP
Formal Name	N-[5-bromo-1-[(4-fluorophenyl)methyl]-4-methyl-2-oxo-3-pyridyl]cyclohexanecarboxamide
InChI Key	CKYYASUICQFJPH-UHFFFAOYSA-N
CAS Number	Not Available
Chemical Formula	$C_{20}H_{22}BrFN_2O_2$
Molecular Weight	421.30
Molecular Ion [M$^+$]	420
Exact Mass [M+H]$^+$	421.0921

Page 1 of 7

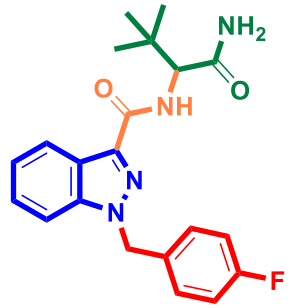
CHO-4'Me-5'Br-FUBOXPYRA

Item No. 37468



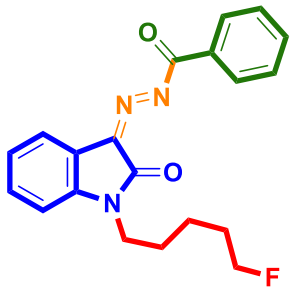
https://www.cfsre.org/nps-discovery/monographs/cho-4me-5br-fuboxpyra

Synthetic cannabinoid naming codes



ADB-FUBINACA

N-(1-**A**mino-3,3-**D**imethyl-1-oxo**B**utan-2-yl)-1-(4-**FU**oro**B**enzyl)-1*H*-**IN**d**A**zole-3-**C**arbox**A**mide

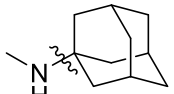


5F-BZO-POXIZID

N'-(1-(**5-F**luoro**P**entyl)-2-**OX**o**I**ndolin-3-ylidene)**B**en**ZO**hydra**ZID**e

Head Groups:

A =



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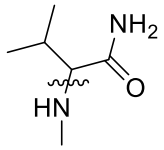
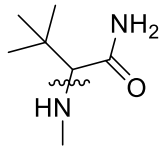


ADB = except: MAB-CHMINACA



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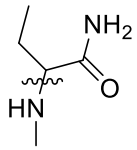

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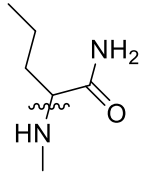

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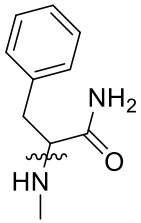

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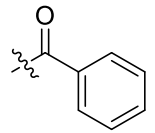

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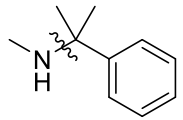

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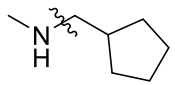
CPM =



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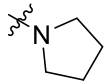

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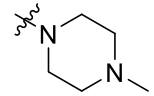

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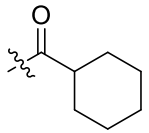

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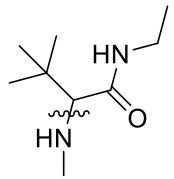

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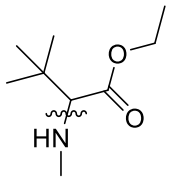
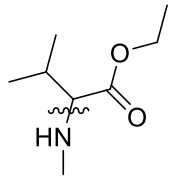


EMB = Also: AEB



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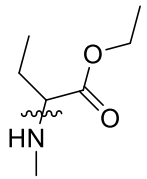

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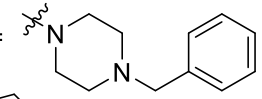
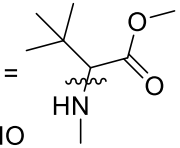
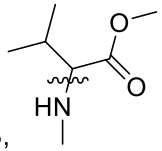


MDMB = Also: ADB, MO



MMB = Also: MAB, AMB, MA



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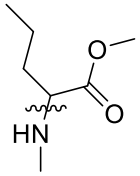

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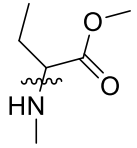
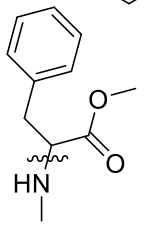
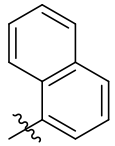


MPP = Also: MPhP



NA = Also: NE



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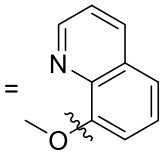
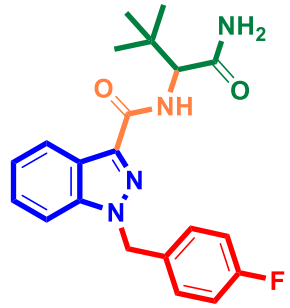


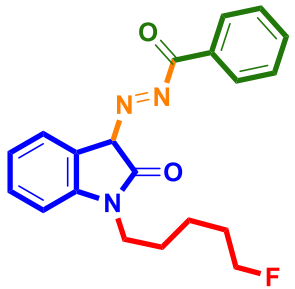
Head-TailCoreLinker

Synthetic cannabinoid naming codes



ADB-FUBINACA

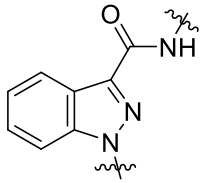
N-(1-Amino-3,3-Dimethyl-1-oxoButan-2-yl)-1-(4-FluoroBenzyl)-1*H*-INdAzole-3-CarboxAmide

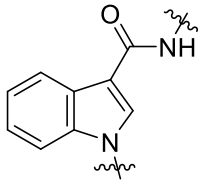


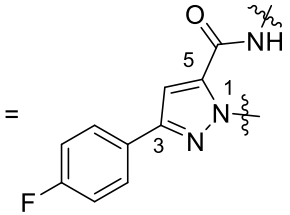
5F-BZO-POXIZID

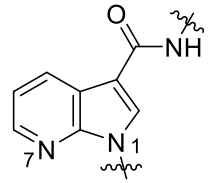
N'-(1-(5-FluoroPentyl)-2-OXoIndolin-3-ylidene)BenZOhydraZIDe

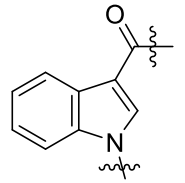
CoreLinkers:

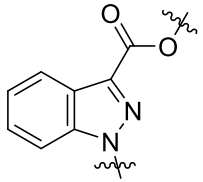
INACA = 

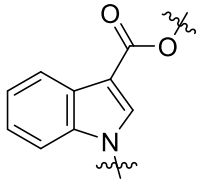
ICA = 

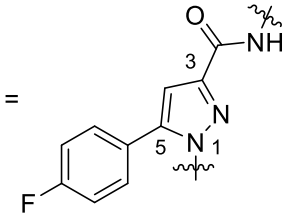
3,5-FUPPYCA = Also: FUPYCA, FUPPYCA 

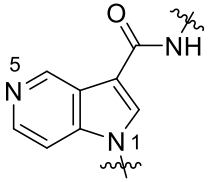
7AICA = 

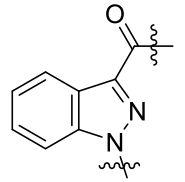
IM = 

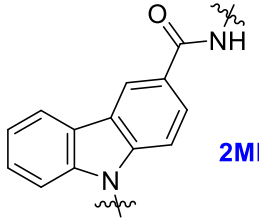
INAC = 

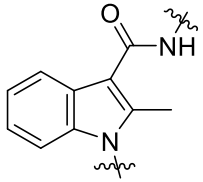
IC = 

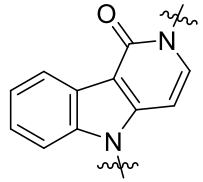
5,3-FUPPYCA = 

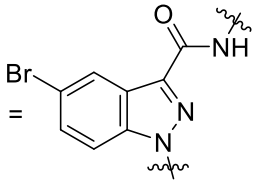
5AICA = 

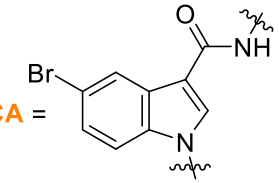
INAM = 

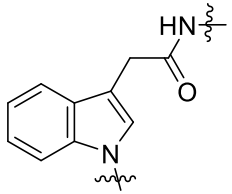
CZCA = 

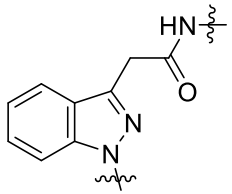
2MICA = 

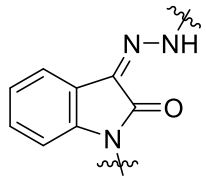
GACLONE = 

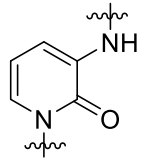
5Br-INACA = 

5Br-ICA = 

IATA = 

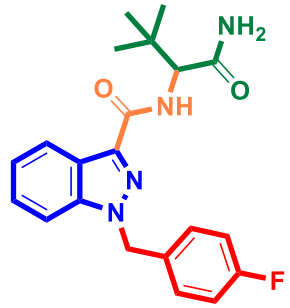
INAATA = 

OXIZID = 

OXPYRA = 

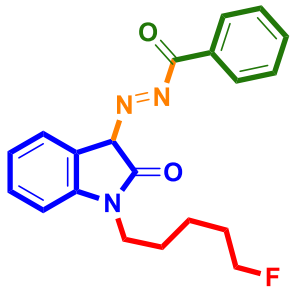
Head-TailCoreLinker

Synthetic cannabinoid naming codes



ADB-FUBINACA

N-(1-**A**mino-3,3-**D**imethyl-1-oxo**B**utan-2-yl)-1-(4-**FU**oro**B**enzyl)-1*H*-**IN**d**A**zole-3-**C**arbox**A**mide



5F-BZO-POXIZID

N'-(1-(**5-F**luoro**P**entyl)-2-**OX**o**I**ndolin-3-ylidene)**B**en**ZO**hydra**ZID**e

Tail Groups:

CPRM =

CBM =
Also:
CB-Me

CPM =

CHM =
Also:
CH,
CH-Me

NBM =
Also:
BC-Hp,
BC-HpM

BUT =
Also:
B

3en-BUT =

4CN BUT =
Also:
CYB, CB-P

4F-BUT =
Also:
4F-B

BENZ =
Also:
B

FUB =

P =
Also:
Pe

4en-P =
Also:
PEN

5F, **5Cl**, **5Br-P** =
F, Cl, Br

PHET =

PIPET =

THP =

DEC =
Also:
D

9en-DEC =

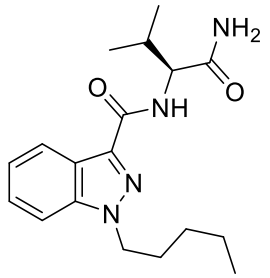
HEX =
Also:
H

HEPT =

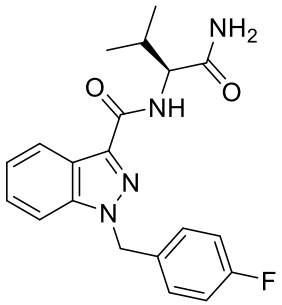
Head-TailCoreLinker

The big question:

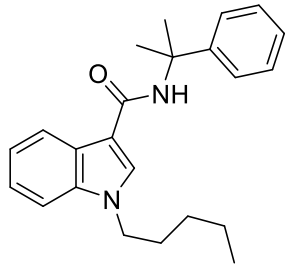
How do I possibly keep track of all the letter codes for the Head, Tail, Core and Linker groups for all theses syn canns?



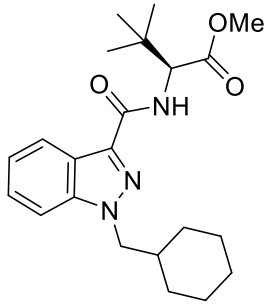
AB-PINACA



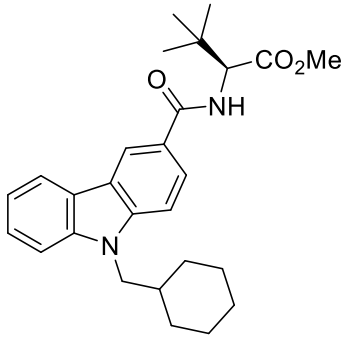
AB-FUBINACA



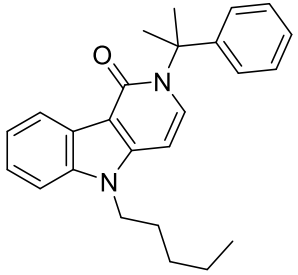
CUMYL-PICA



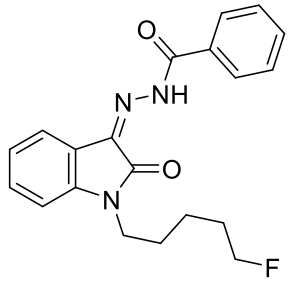
MDMB-CHMINACA



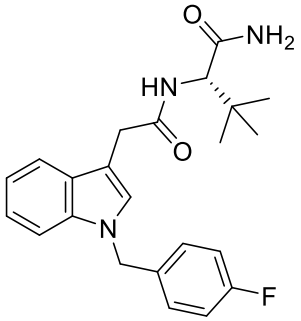
MDMB-CHMCZCA



CUMYL-PEGACLONE

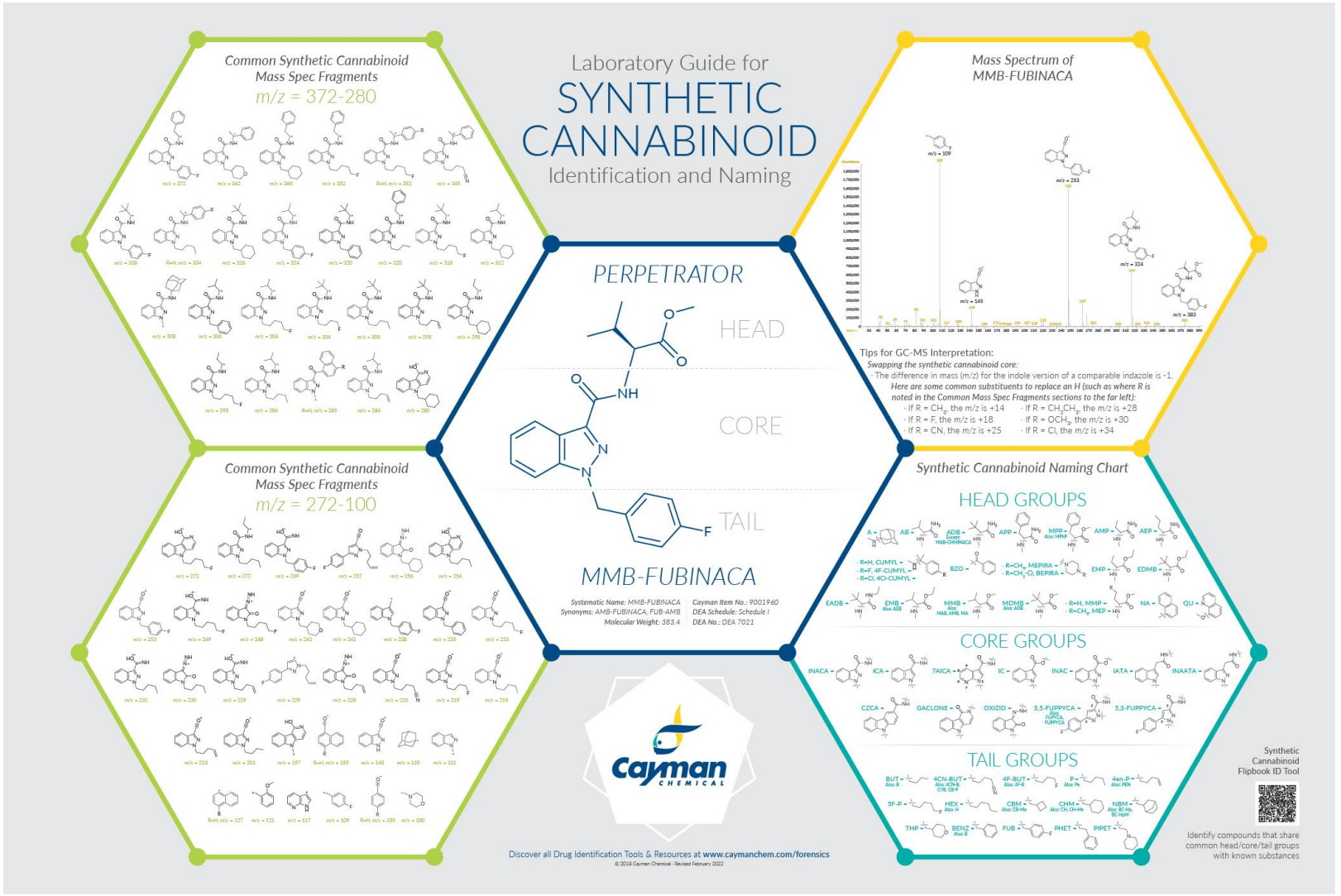


5F-BZO-POXIZID



ADB-FUBIATA

Synthetic cannabinoid lab guide poster



https://www.caymanchem.com/literature/laboratory-guide-for-synthetic-cannabinoid-identification-and-naming

Recent EMCDDA publication on naming guidelines

DRUG TESTING AND ANALYSIS

PERSPECTIVE

EMCDDA framework and practical guidance for naming synthetic cannabinoids

Benedikt Pulver, Svenja Fischmann ✉, Ana Gallegos, Rachel Christie

First published: 08 November 2022 | https://doi.org/10.1002/dta.3403

- Provides a theoretical framework and a practical hands-on guideline for consistent naming of SCs
- Builds on the established letter code system for molecular building blocks (core, linker, linked group, and tail)
- The scope of the issue of attributing semi-systematic code names is illustrated and earlier approaches used for naming SCs are discussed
- There is some overlap with our approach, but not always

Naming agreements and reaching a consensus

- Consideration for naming conventions:
  - Primary goal – create less confusion
  - Consider historical perspectives
  - Communication – both verbal and written
  - Forecasting the future

- Examples of Cayman/CFSRE naming vs. EMCDDA:
  - BZO-4en-POXIZID vs. BZO-4en-POXIZID
  - ADB-FUBIATA vs. ADMB-FUBIATA
  - 5F-MDMB-PICA vs. MDMB-5F-PICA
  - JWH-210 vs. 4Et-NA-PIMO

Future Directions

- CFSRE and Cayman Chemical received funded by the National Institute of Justice (NIJ) to continue work on naming conventions:

- In the works:
  - Synthetic cannabinoid
  - Fentanyl analogue
  - Nitazene analogue

- Other opportunities:
  - Cathinones
  - Hallucinogens

Thank You!

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alex.krotulski@cfsre.org

cfsre