

Changes in the prevalence of new psychoactive substances before and after the introduction of the generic scheduling of synthetic cannabinoids in Japan

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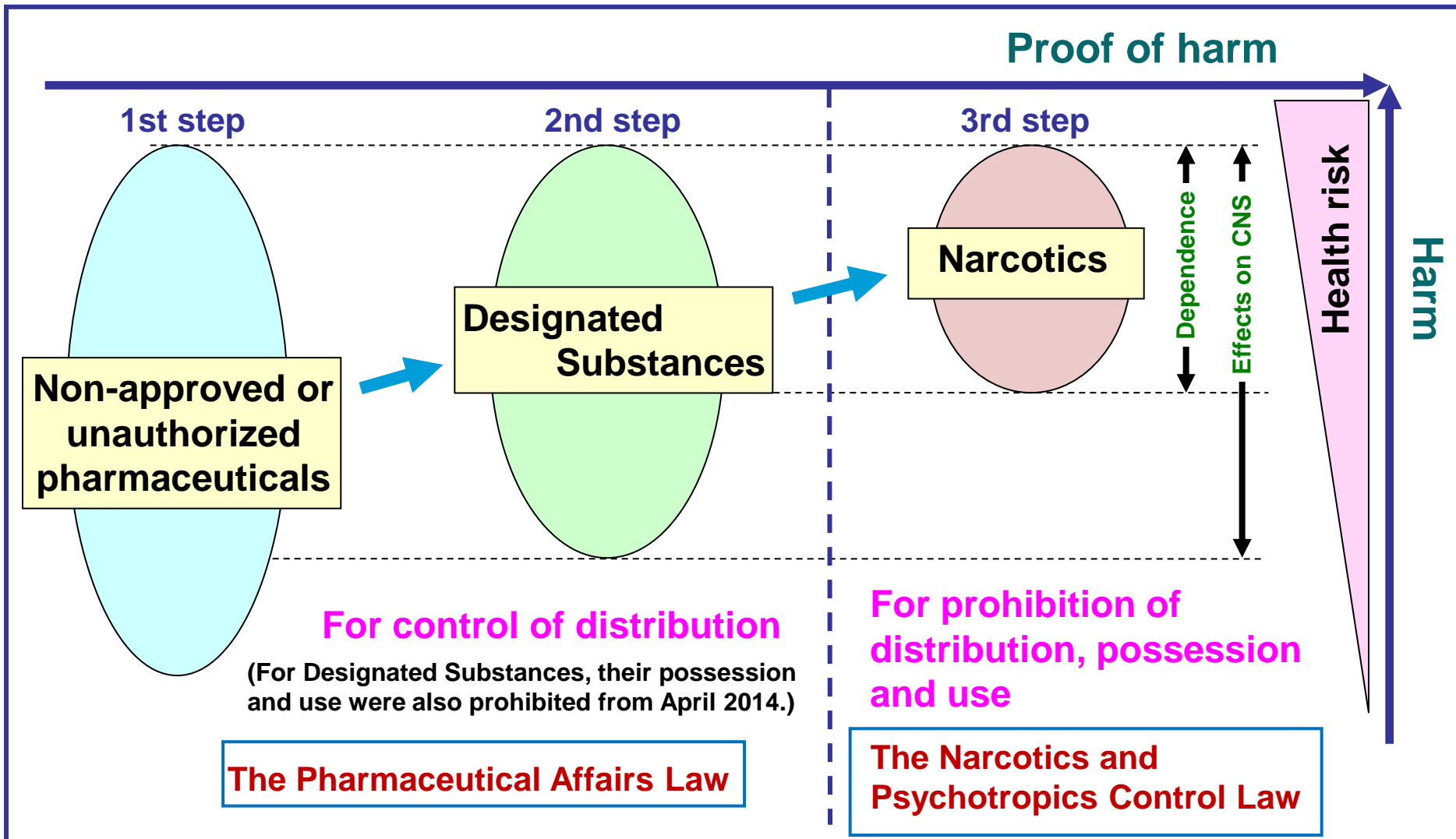
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Introduction of “Designated Substances” into the Pharmaceutical Affairs Law in 2007



Since 2011...

- ✓ Serious health damage (including fatal cases) and car accidents related to “herbal products” or “aroma liquids” have increased.



Various products (Photo in 2013)



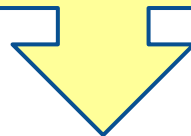
Sheet-type products containing 25I- or 25C-NBOMe (Photo in 2013)

Vending machine for “herbal products” (Photo in 2012, the machine was removed)



Countermeasures against various analogs of psychotropic substances

New analogs of psychoactive substances have appeared one after the other.

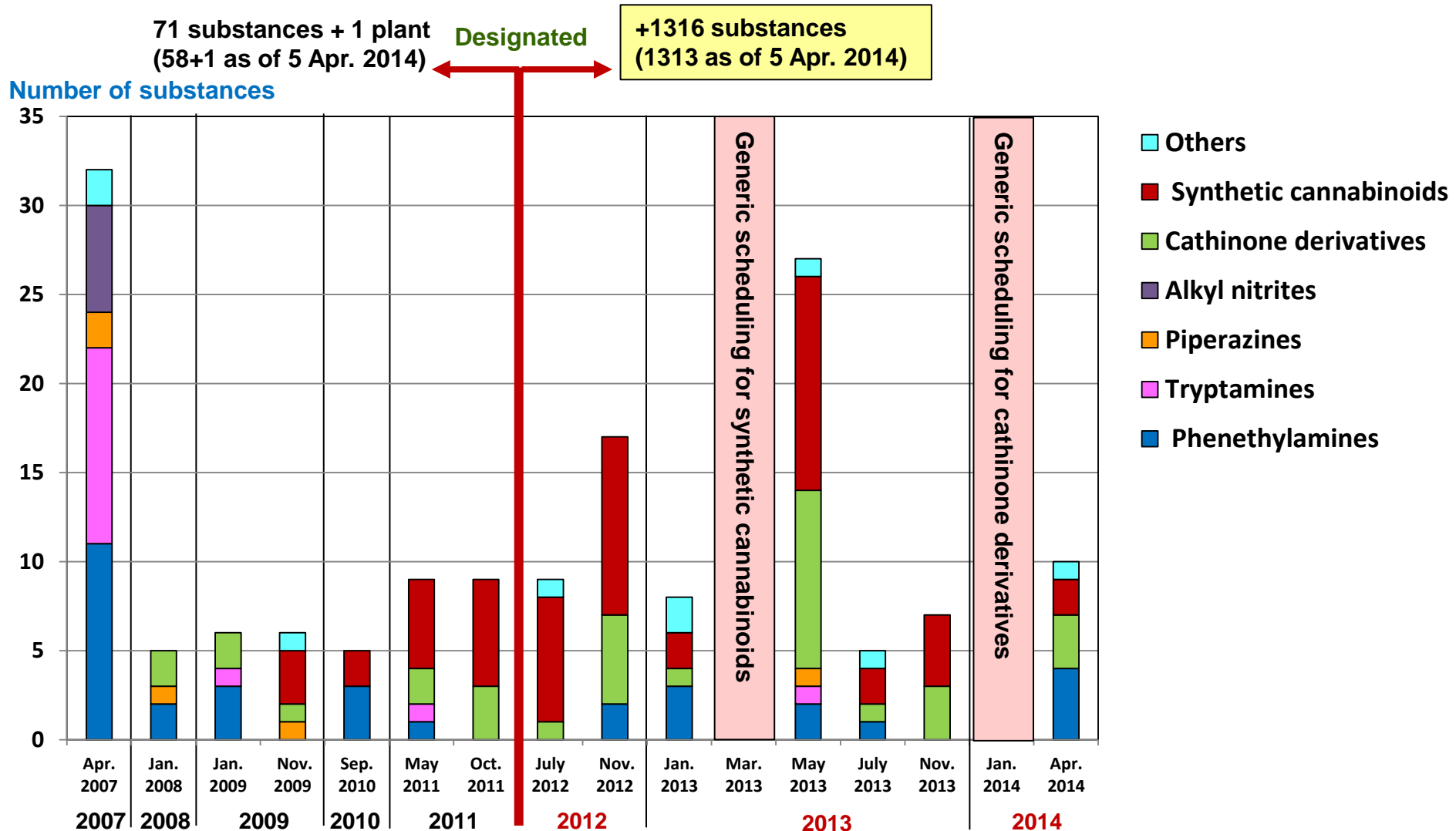


For their scheduling,

the Ministry of Health, Labor and Welfare

- 1. listing new psychoactive substances as Designated Substances with greater speed.**
- 2. speedily re-categorizing Designated Substances into Narcotics.**
- 3. introducing generic scheduling.**

1. Greater speed in listing new psychoactive substances as Designated Substances



Designated Substances : 1370 substances + 1 plant (*Salvia divinorum*) as of 1 May 2014

2. Designated Substances speedily re-categorized into Narcotics

18 Jun. 2008	2C-I, 2C-T-2, 2C-T-4	
3 August 2012	Cannabicyclohexanol, JWH-018, MDPV, Mephedrone	
1 March 2013	PMMA, 5-MeO-DALT, Ethcathinone α -PVP, JWH-073, JWH-122	
26 May 2013	AM-2201, MAM-2201	14 substances from 2012
19 Jan. 2014	bk-MDEA, XLR-11	



Designated Substances



Narcotics

Much stricter control

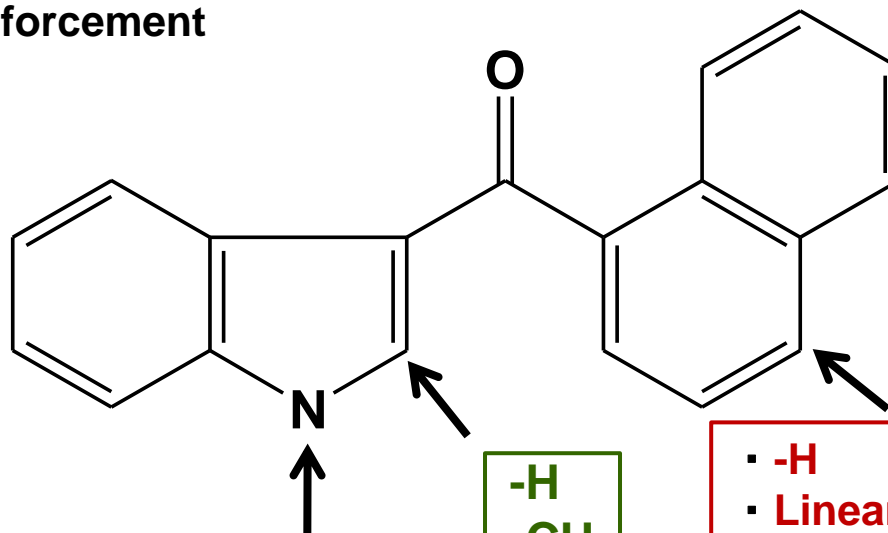
Phenethylamines
Tryptamines
Cathinones
Synthetic cannabinoids

3. Introduction of generic scheduling

Naphthoylindoles

20th Feb. 2013 Promulgation of a ministerial order

22nd Mar. 2013 Enforcement



- Linear alkyl groups (C3-C8)
- Alkenyl groups (C-5)
- Linear alkyl groups (C3-C5)
+ terminal -F, -Cl, -Br, -I
-CN, -OH, -COOCH₃

* There are some exclusions.

-H
-CH₃

- -H
- Linear alkyl groups (C1-C6)
- -OCH₃, -OCH₂CH₃
- -F, -Cl, -Br, -I

* There are some exclusions.

Total 775 substances

- 5 Narcotics

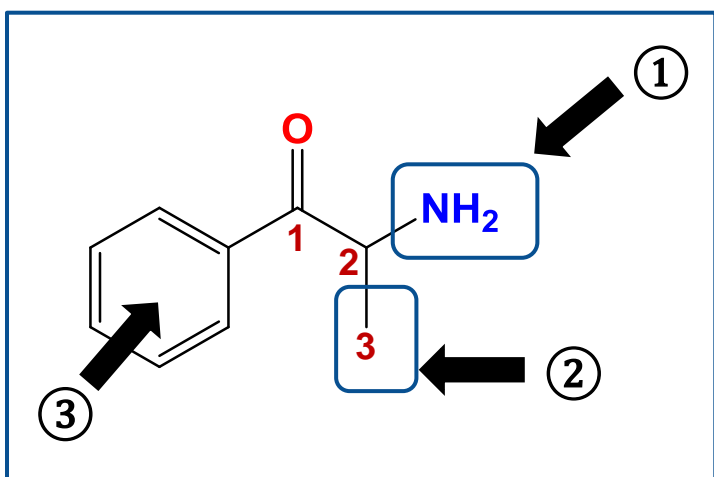
- 11 Designated Substances

➡ 759 New additional Designated Substances

Cathinone derivatives

13th Dec. 2013 Promulgation of a ministerial order

12th Jan. 2014 Enforcement



①	②	③
methylamino	methyl	methyl
ethylamino	ethyl	ethyl
dimethylamino	propyl	methoxy
diethylamino		methylenedioxy
ethylmethylamino		F
1-pyrrolidinyl		Cl
ethylamino		Br
		I

Total 504 substances

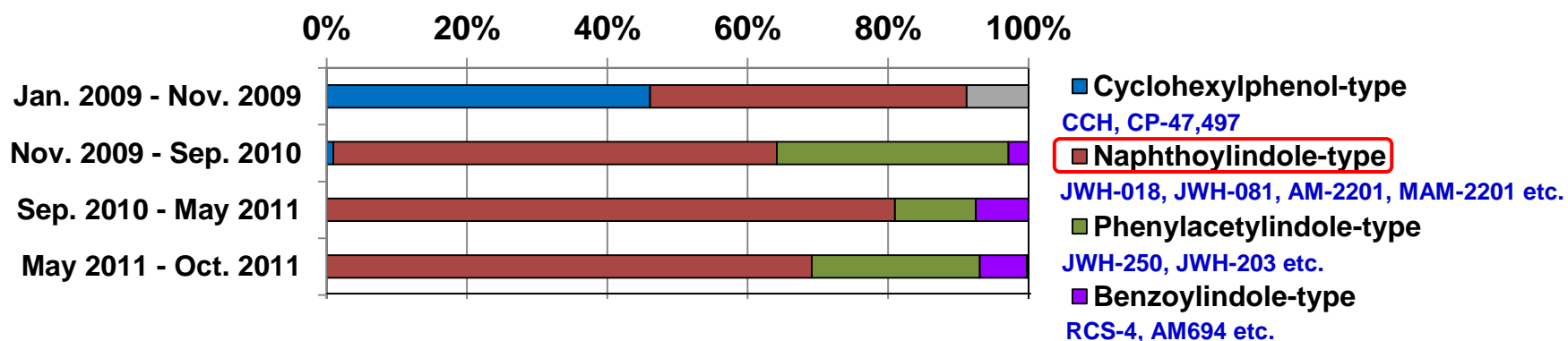
- 7 Narcotics
- 2 Psychotropics
- 21 Designated Substances

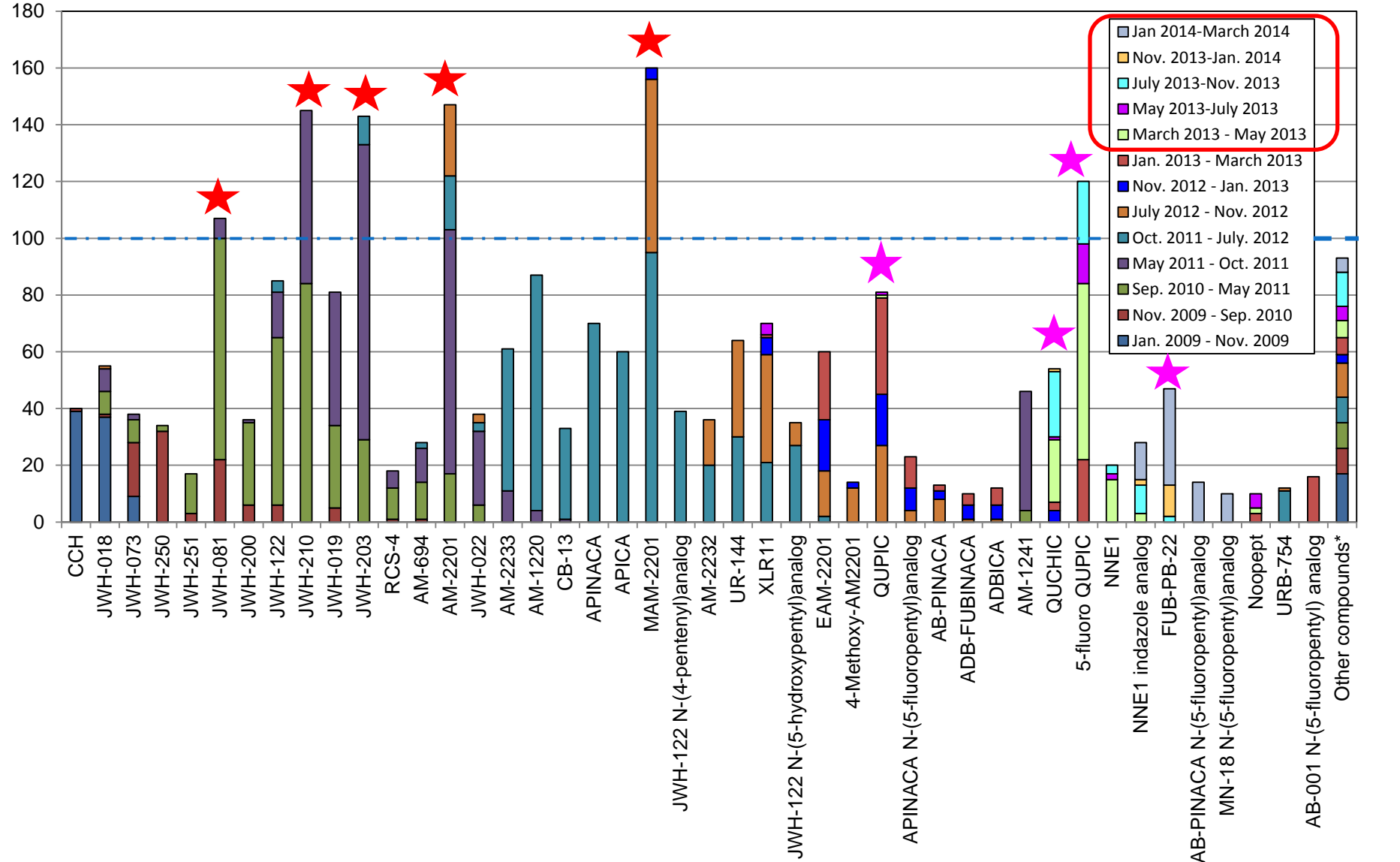
➡ **474 New additional Designated Substances**

Changes in the prevalence of NPS before and after the introduction of the generic scheduling

Changes in structures of synthetic cannabinoids

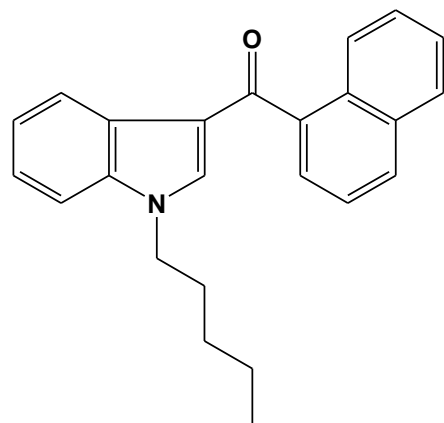
The ratio of synthetic cannabinoids having various structures detected in the products
(from Jan. 2009 to March 2014, 1433 products)



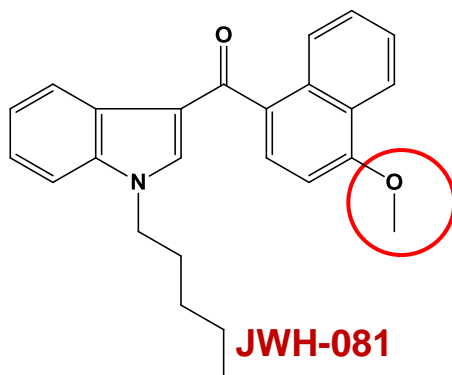


The prevalence of naphthoylindole-type synthetic cannabinoids

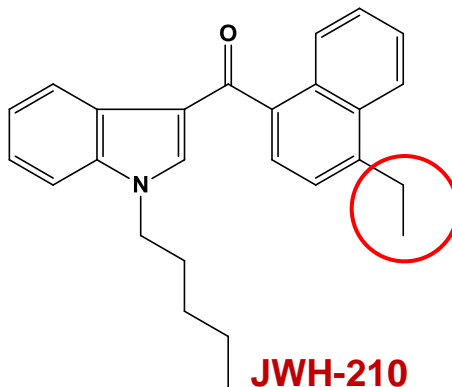
**TOP 5
(from 2009 to 2012)**



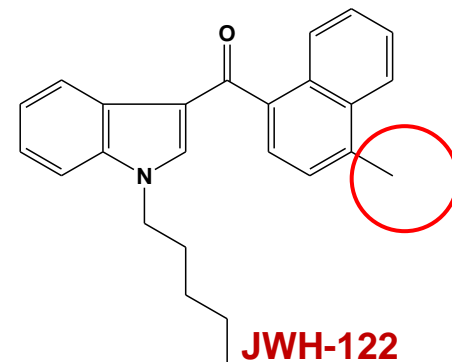
JWH-018



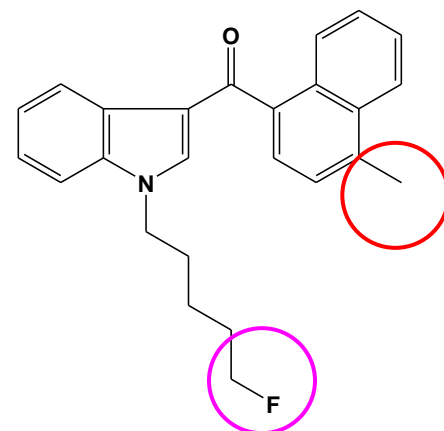
JWH-081



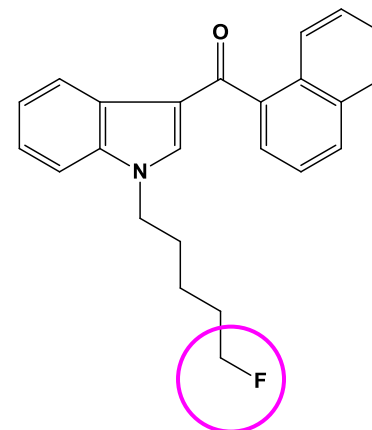
JWH-210



JWH-122

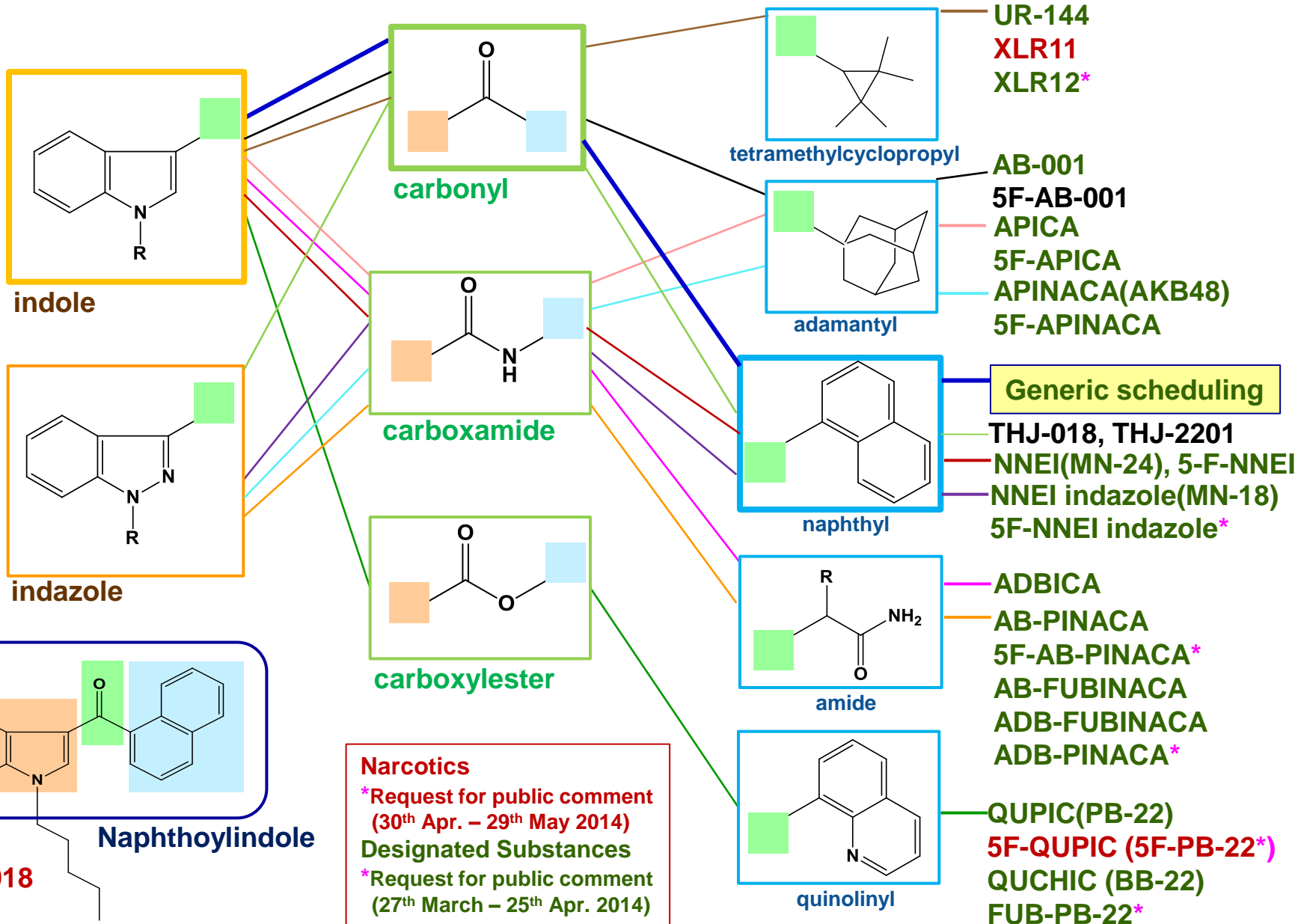


MAM-2201

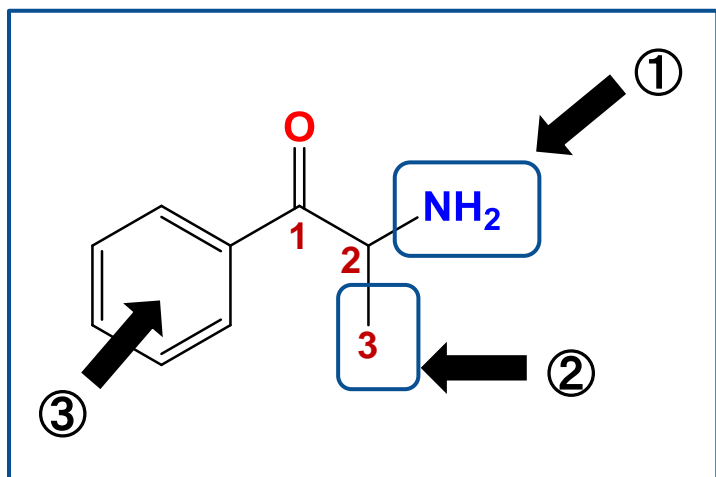


AM-2201

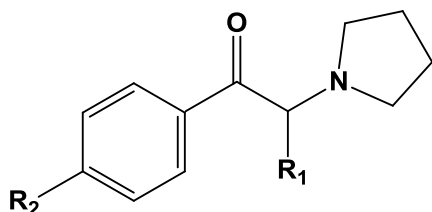
The emergence of new types of synthetic cannabinoids



The emergence of new types of cathinone derivatives



①	②	③
methylamino	methyl	methyl
ethylamino	ethyl	ethyl
dimethylamino	propyl	methoxy
diethylamino		methylenedioxy
ethylmethylamino		F
1-pyrrolidinyl		Cl
ethylamino		Br
		I



$R_1 = -C_4H_9$ **α -PHP**
 $R_1 = -C_5H_{11}$ **α -PHPP (PV8)** Nov 2013 DS
 $R_1 = -C_6H_{13}$ **α -POP (PV9)** April 2013 DS
 $R_2 = H, \text{methyl, methoxy, fluoro}$



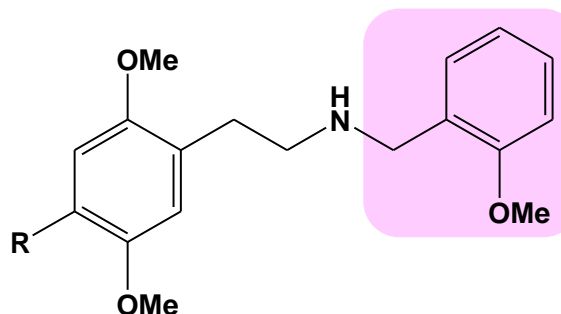
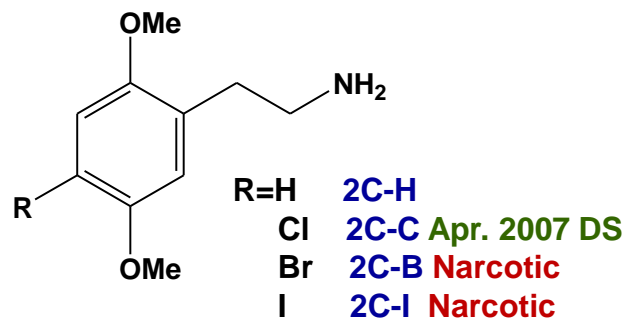
Generic scheduling

①	②	③
1-piperidinyl	butyl	dimethoxy
	heptyl	dimethyl
	octyl	

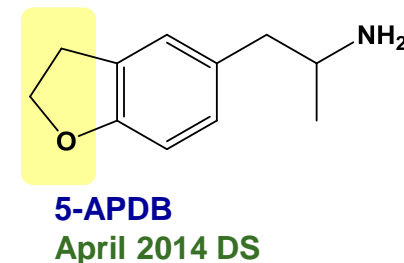
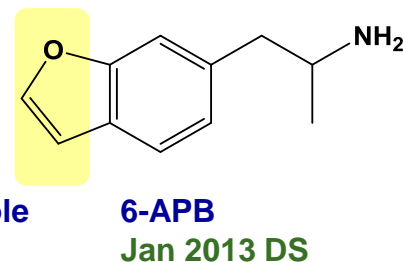
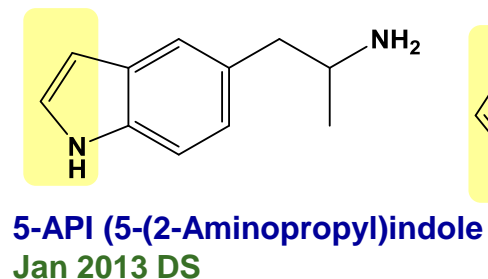
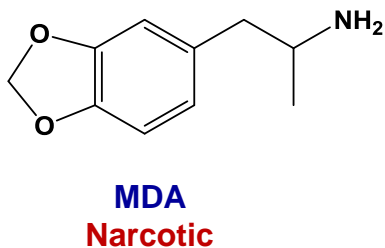
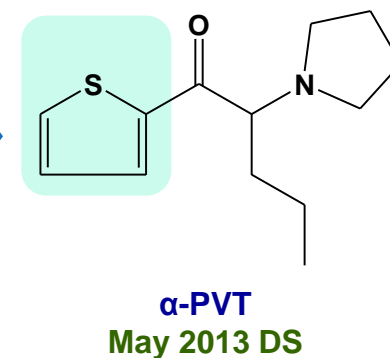
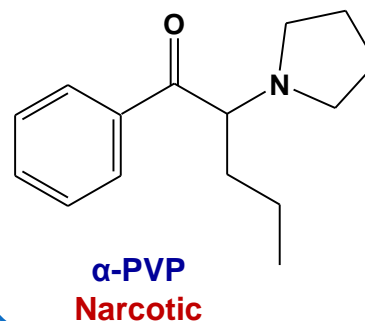
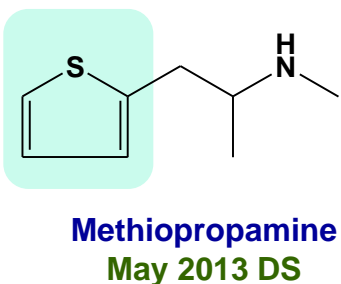
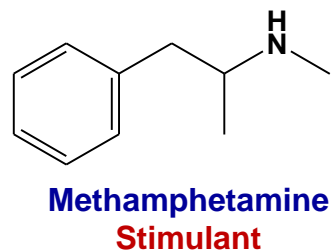
Other new psychoactive substances from 2012

1

DS: Designated Substances



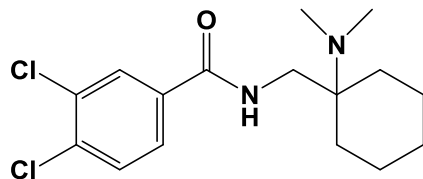
$R=H$ **25H-NBOMe** Apr. 2014 DS
 Cl **2C-C-NBOMe** Jan. 2013 DS
 (25C-NBOMe)
 Br **25B-NBOMe** Apr. 2014 DS
 I **25I-NBOMe** Nov. 2012 DS
 NO_2 **2C-N-NBOMe**



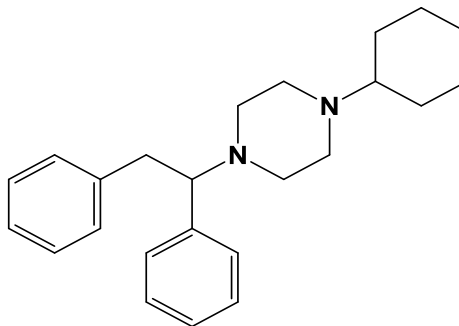
Other new psychoactive substances from 2012

2

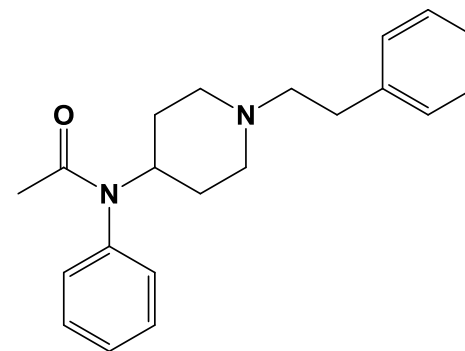
Opioid receptor agonists

**AH-7921**

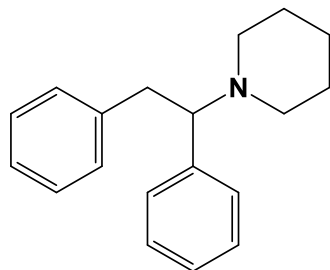
July 2013 DS

**MT-45**

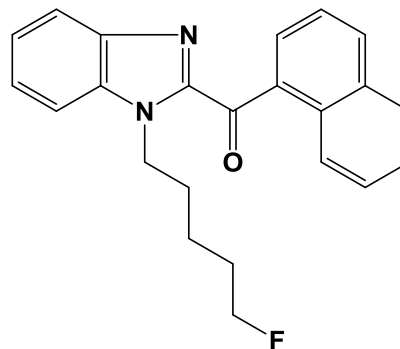
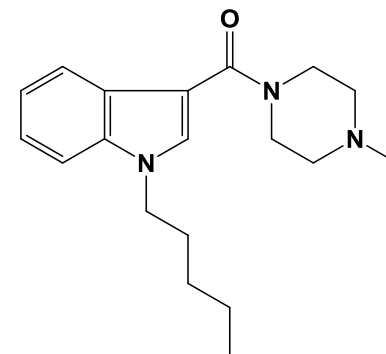
July 2013 DS

**Acetyl fentanyl**Request for public comment
(27th March to 25th April 2014)

NMDA receptor antagonist

**Diphenidine**

Other types of synthetic cannabinoids

**AM-2201 benzimidazole
(FUBIMINA)****MEPIRAPIM****DS: Designated Substances**

Data Search System for New Psychoactive Substances by the NIHS since March 2014

http://npsdb.nihs.go.jp/Search/Default_e.aspx

It provides information on

- ✓ chemical properties, analytical data and pharmacological properties of NPS.
(**543 substances** as of March 2014)
- ✓ herbal, aroma liquid or powdery products sold in Japan, including their photos, product names, forms and detected substances.
(**1785 products** as of March 2014)

For registration, send an e-mail to
npsdpp3@nihs.go.jp or **kikura@nihs.go.jp**

Thank you for your attention

Our recent publications related to NPS

R. Kikura-Hanajiri et al., *Drug Test. Anal.*, in press, DOI 10.1002/dta.1584.

N. Uchiyama et al., *Forensic Sci Int*, 243, 1–13 (2014).

N. Uchiyama et al., *Forensic Toxicology*, 32, 105–115 (2014).

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N. Uchiyama et al., *Forensic Sci Int.*, 215(1–3), 179–183 (2012).

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N. Uchiyama et al., *Yakugaku Zasshi*, 131(7), 1141–1147 (2011).

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R. Kikura-Hanajiri et al., *Yakugaku Zasshi*, 128(6), 971–979 (2008).

R. Kikura-Hanajiri et al., *J. Chromatogra. B.*, 855(2), 121–126 (2007).

R. Kikura-Hanajiri et al., *J. Chromatogra. B.*, 825(1), 29–37 (2005).

