



Synthetic Substances – DEA Request for Information

The emergence of synthetic substances on the designer drug market in the United States is of great concern. These substances are sold at smoke shops, head shops, convenience stores, adult book stores, and gas stations and can also be purchased on the Internet. These substances are being abused for their psychoactive properties and are packaged without information as to their health and safety risks.

Synthetic Cannabinoids

Synthetic cannabinoids are a large family of substances that mimic functionally (biologically) the effects of the structurally unrelated delta-9-tetrahydrocannabinol (THC), a Schedule I substance, and the main active ingredient of marijuana. Synthetic cannabinoids have been marketed under the guise of “herbal incense,” and promoted by drug traffickers as legal alternatives to marijuana.

Recently, legislation regarding many of these substances was enacted making the manufacturing, distribution, dispensing, and possession of these substances illegal. On July 9, 2012, President Obama signed the Food and Drug Administration Safety and Innovation Act (FDASIA), which amended several provisions of the Controlled Substances Act (CSA). The “Synthetic Drug Abuse Prevention Act of 2012,” (SDAPA), Pub. L. 112-144, Title XI, subtitle D, amended section 202 of the CSA by adding cannabimimetic agents to Schedule I. The term “cannabimimetic agents” was defined to include substances within defined structural classes that are demonstrated by binding studies and functional assays to be cannabinoid receptor type 1 (CB1 receptor) agonists. The SDAPA also added 15 specific cannabimimetic agents to Schedule I of section 202(c) of the CSA. On May 16, 2013, three synthetic cannabinoids, UR-144, XLR11 and AKB48 were emergency scheduled and placed into Schedule I of the CSA. In addition, on February 10, 2014, four additional cannabinoids, PB-22, 5F-PB-22, AB-FUBINACA and ADB-PINACA were also emergency scheduled and placed into Schedule I of the CSA.

1. **AKB48**, chemical name: *N*-(1-adamantyl)-1-pentyl-1*H*-indazole-3-carboxamide
2. **XLR-11**, chemical name: (1-(5-fluoropentyl)-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone
3. **UR-144**, chemical name: (1-pentyl-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone
4. **PB-22 (QUPIC)**, chemical name: quinolin-8-yl 1-pentyl-1*H*-indole-3-carboxylate
5. **5F-PB-22**, chemical name: quinolin-8-yl 1-(5-fluoropentyl)-1*H*-indole-3-carboxylate
6. **AB-FUBINACA**, chemical name: *N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1*H*-indazole-3-carboxamide
7. **ADB-PINACA**, chemical name: *N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1*H*-indazole-3-carboxamide

Newer generations of synthetic cannabinoid substances (i.e., synthetic cannabinoid substances that are not listed in the CSA), as evidenced by law enforcement encounters, are emerging in the U.S. illicit drug market. There is little, if any, pharmacological information regarding these substances. Some of these substances include, but are not limited to:

8. **5F-AKB48**, chemical name: *N*-(1-adamantyl)-1-(5-fluoropentyl)-1*H*-indazole-3-carboxamide
9. **STS-135**, chemical name: *N*-(adamantan-1-yl)-1-(5-fluoropentyl)-1*H*-indole-3-carboxamide
10. **AB-001**, chemical name: adamantan-1-yl(1-pentyl-1*H*-indol-3-yl)methanone
11. **2NE1 (AKA: APICA; SDB-001)**, chemical name: *N*-(adamantan-1-yl)-1-pentyl-1*H*-indole-3-carboxamide
12. **NNE-1**, chemical name: *N*-(naphthalen-1-yl)-1-pentyl-1*H*-indole-3-carboxamide
13. **AB-PINACA**, chemical name: *N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-pentyl-1*H*-indazole-3-carboxamide
14. **ADB-FUBINACA**, chemical name: *N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(4-fluorobenzyl)-1*H*-indazole-3-carboxamide
15. **ADBICA**, chemical name: *N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1*H*-indole-3-carboxamide
16. **AB-CHMINACA**, chemical name: *N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(cyclohexylmethyl)-1*H*-indazole-3-carboxamide
17. **A-834,735**, chemical name: (1-[(tetrahydro-2*H*-pyran-4-yl)methyl]-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone
18. **FUBIMINA**, chemical name: (1-(5-fluoropentyl)-1*H*-benzo[*d*]imidazol-2-yl)(naphthalen-1-yl)methanone
19. **JWH-018 benzimidazole analog**, chemical name: naphthalen-1-yl(1-pentyl-1*H*-benzo[*d*]imidazol-2-yl)methanone
20. **MEPIRAPIM (AKA: JWH-018-4(methylpiperazine))**, chemical name: (4-methylpiperazin-1-yl)(1-pentyl-1*H*-indol-3-yl)methanone
21. **THJ-018**, chemical name: naphthalen-1-yl(1-pentyl-1*H*-indazol-3-yl)methanone
22. **THJ-2201**, chemical name: (1-(5-fluoropentyl)-1*H*-indazol-3-yl)(naphthalen-1-yl)methanone
23. **FUB-PB-22**, chemical name: quinolin-8-yl 1-(4-fluorobenzyl)-1*H*-indole-3-carboxylate
24. **BB-22**, chemical name: quinolin-8-yl 1-(cyclohexylmethyl)-1*H*-indole-3-carboxylate
25. **FDU-PB-22**, chemical name: naphthalen-1-yl 1-(4-fluorobenzyl)-1*H*-indole-3-carboxylate
26. **EG-018**, chemical name: naphthalen-1-yl(9-pentyl-9*H*-carbazol-3-yl)methanone
27. **5F-AB-PINACA**, chemical name: *N*-(1-amino-3-methyl-1-oxobutan-2-yl)-1-(5-fluoropentyl)-1*H*-indazole-3-carboxamide
28. **FUB-144**, chemical name: (1-(4-fluorobenzyl)-1*H*-indol-3-yl)(2,2,3,3-tetramethylcyclopropyl)methanone
29. **5F-ADBICA**, chemical name: *N*-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-(5-fluoropentyl)-1*H*-indole-3-carboxamide

Other Synthetic Substances

In addition to the synthetic cannabinoids, other classes of synthetic substances have emerged in the U.S. illicit drug market as evidenced by law enforcement encounters. These substances include various subclasses of phenethylamines, arylcyclohexylamines, substituted tryptamines, and other chemical class structures.

Phenethylamines (2C series)

Historically, a number of substances from this class of compounds have been abused for their psychoactive properties.

On July 9, 2012, the SDAPA amended Schedule I of the CSA to include a number of synthetic substances with a phenethylamine core structure (2-(2,5-dimethoxy-4-ethylphenyl)ethanamine (2C-E), 2-(4-iodo-2,5-dimethoxyphenyl)ethanamine (2C-I), etc.). However, as evidenced by law enforcement encounters, other phenethylamine substances are emerging in the U.S. illicit drug market. Thus, on November 15, 2013, three synthetic phenethylamines were emergency scheduled and placed into Schedule I of the CSA. There is limited pharmacological information regarding the three emergency scheduled substances and other newly emerging substances.

30. **25I-NBOMe**, chemical name: 2-(4-iodo-2,5-dimethoxyphenyl)-*N*-(2-methoxybenzyl)ethanamine
31. **25B-NBOMe**, chemical name: 2-(4-bromo-2,5-dimethoxyphenyl)-*N*-(2-methoxybenzyl)ethanamine
32. **25C-NBOMe**, chemical name: 2-(4-chloro-2,5-dimethoxyphenyl)-*N*-(2-methoxybenzyl)ethanamine

Cathinones

Synthetic cathinones have been falsely marketed as “research chemicals,” “jewelry cleaner,” “stain remover,” “plant food or fertilizer,” insect repellants,” or “bath salts.” These substances are being abused for their stimulant effects. Many synthetic cathinones have been shown to possess pharmacological properties similar to the Schedule I substances cathinone, methcathinone, and 3,4-methylenedioxymethamphetamine (MDMA) and Schedule II stimulants amphetamine, methamphetamine, and cocaine.

On July 9, 2012, the SDAPA amended Schedule I of the CSA to include the synthetic cathinones mephedrone and 3,4-methylenedioxypyrovalerone (MDPV). Methylone was permanently controlled via the administrative scheduling process on April 12, 2013. On March 7, 2014, 10 additional synthetic cathinones were emergency scheduled and placed into Schedule I of the CSA. There is limited pharmacological information regarding these substances.

33. **4-MEC**, chemical name: 4-methyl-*N*-ethylcathinone
34. **4-MePPP**, chemical name: 4-methyl- α -pyrrolidinopropiophenone
35. **α -PVP**, chemical name: α -pyrrolidinopentiophenone
36. **Butylone**, chemical name: 1-(1,3-benzodioxol-5-yl)-2-(methylamino)butan-1-one
37. **Pentadrone**, chemical name: 2-(methylamino)-1-phenylpentan-1-one
38. **Pentylone**, chemical name: 1-(1,3-benzodioxol-5-yl)-2-(methylamino)pentan-1-one
39. **Flephedrone**, chemical name: 4-fluoro-*N*-methylcathinone, synonym 4-FMC
40. **3-FMC**, chemical name: 3-fluoro-*N*-methylcathinone
41. **Naphyrone**, chemical name: naphthylpyrovalerone, synonym: NRG-1
42. **α -PBP**, chemical name: α -pyrrolidinobutiophenone

The next generation of synthetic cathinone substances, as evidenced by law enforcement encounters, is emerging in the U.S. illicit drug market. There is little, if any, pharmacological information regarding these substances. Some of these substances include but are not limited to:

- 43. **MDPBP**, chemical name: 3',4'-methylenedioxy- α -pyrrolidinobutiophenone
- 44. **MPHP**, chemical name: 4'-methyl- α -pyrrolidinohexanophenone
- 45. **MDPPP**, chemical name: 3',4'-methylenedioxy- α -pyrrolidinopropiophenone
- 46. **Dimethylone**, chemical name: *N,N*-dimethyl-3',4'-methylenedioxycathinone
- 47. **Ethylone**, chemical name: 3',4'-methylenedioxy-*N*-ethylcathinone

Benzofurans

Benzofurans are another class of substances that share a phenethylamine core structure and have been reported to produce hallucinogenic effects. These substances, as evidenced by law enforcement encounters, are emerging in the U.S. illicit drug market. There is limited pharmacological information regarding these substances. Some of these substances include but are not limited to:

- 48. **5-APB**, chemical name: 1-(benzofuran-5-yl)propan-2-amine
- 49. **5-APDB**, chemical name: 1-(2,3-dihydrobenzofuran-5-yl)propan-2-amine
- 50. **6-APB**, chemical name: 1-(1-benzofuran-6-yl)propan-2-amine
- 51. **6-APDB**, chemical name: 1-(2,3-dihydrobenzofuran-6-yl)propan-2-amine

Arylcyclohexylamines

Arylcyclohexylamines encompass a group of synthetic psychoactive substances which are structurally and pharmacologically related to phencyclidine (PCP), a Schedule II drug, and *N*-ethyl-1-phenylcyclohexylamine (PCE), a Schedule I drug. There has been an increase in the law enforcement encounters of the below mentioned arylcyclohexylamines. There is limited pharmacological information regarding these substances.

- 52. **Methoxetamine**, chemical name: 2-(ethylamino)-2-(3-methoxyphenyl)cyclohexanone
- 53. **3-methoxy-PCE**, chemical name: *N*-ethyl-1-(3-methoxyphenyl)cyclohexylamine
- 54. **3-methoxy-PCP**, chemical name: 1-[1-(3-methoxyphenyl)cyclohexyl]piperidine
- 55. **4-methoxy-PCP**, chemical name: 1-[1-(4-methoxyphenyl)cyclohexyl]piperidine

Tryptamines

Tryptamines are abused for their hallucinogenic-like effects. There has been an increase in the law enforcement encounters of the below mentioned tryptamines. There is little, if any, pharmacological information regarding these substances.

- 56. **5-MeO-DALT**, chemical name: *N,N*-diallyl-5-methoxytryptamine
- 57. **4-AcO-DMT**, chemical name: 5-acetoxy-*N,N*-dimethyltryptamine

The Drug and Chemical Evaluation Section (ODE) of the DEA Office of Diversion Control continues to gather information on the pharmacology, toxicity, and abuse of the above

mentioned synthetic substances and products containing these substances to support possible control under the CSA. ODE would greatly appreciate any information related to law enforcement encounters, drug identification, toxicology reports, medical examiner reports, and abuse related to these substances. This includes, but is not limited to, any information associated with the biological response occurring from episodes, data describing toxic effects from exposure to these substances occurring in humans or animals, toxicology reports, risk assessments, identification of these substances to establish prevalence and trends, and suspicion of poisonings connected to patients or postmortem samples. Information that connects these substances to adverse health effects is of particular interest and would provide valuable assistance in the evaluation of these substances for a federal control action.

Contact Us

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