

FENTANYL-RELATED SUBSTANCES

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DEA/DC/DOE

Introduction:

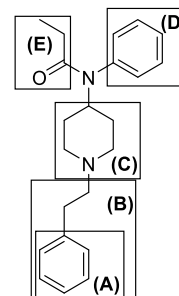
Synthetic opioids, especially those substances related in chemical structure to fentanyl, a potent opioid analgesic with approved medical use, have resulted in an unprecedented number of overdoses in the United States. The recent introduction of synthetic opioids on the illicit market began in 2013 with acetyl fentanyl. The Drug Enforcement Administration (DEA) controlled this substance in schedule I after finding it to be an imminent hazard to the public safety. Following this action, a series of new substances related to fentanyl appeared on the illicit market. From 2015 through February 1, 2018, DEA temporarily controlled 17 substances structurally related to fentanyl in schedule I of the Controlled Substances Act (CSA). During the review process for these 17 substances, information on at least 492 overdose fatalities was collected from a limited number of jurisdictions. Reports¹ from the Centers on Disease Control and Prevention, a component of the Department of Health and Human Services, highlight the increase in mortality attributed to the misuse and abuse of synthetic opioids, to include fentanyl-related substances, in the United States. Following examples of other regulatory authorities expressing public health concerns with the misuse and abuse of synthetic opioids, and in order to protect the public from this accelerating trend, DEA controlled fentanyl-related substances in schedule I as a chemical structural class after finding them to be an imminent hazard to the public safety.

Chemistry:

The term fentanyl-related substance is defined in Title 21 of the Code of Federal Regulations (CFR) § 1308.11(h)(30)(i) as any substance not otherwise listed under another Administration Controlled Substance Code Number, and for which no exemption or approval is in effect under section 505 of the Federal Food, Drug, and Cosmetic Act [21 U.S.C. 355], that is structurally related to fentanyl by one or more of the following modifications:

- (A) replacement of the phenyl portion of the phenethyl group by any monocycle, whether or not further substituted in or on the monocycle;
- (B) substitution in or on the phenethyl group with alkyl, alkenyl, alkoxy, hydroxyl, halo, haloalkyl, amino or nitro groups;
- (C) substitution in or on the piperidine ring with alkyl, alkenyl, alkoxy, ester, ether, hydroxyl, halo, haloalkyl, amino or nitro groups;
- (D) replacement of the aniline ring with any aromatic monocycle whether or not further substituted in or on the aromatic monocycle; and/or
- (E) replacement of the *N*-propionyl group by another acyl group.

The following diagram depicts the regions of the chemical structure of fentanyl described in the definition of a fentanyl-related substance.



Licit Uses and Research:

Fentanyl-related substances, as defined in 21 CFR § 1308.11(h)(30)(i), have no accepted medical use in treatment in the United States. As of May 2020, 27 researchers have applied, and became registered, to conduct research with fentanyl-related substances through the Schedule I Researcher program, demonstrating class control had minimal effect on research. This program allows for scientific research to be conducted with schedule I controlled substances under the United States CSA.

User Population:

The population likely to abuse fentanyl-related substances overlaps with the population abusing prescription opioid analgesics (i.e. oxycodone, hydrocodone), heroin, and fentanyl. Often, fentanyl-related substances are disguised and sold as more traditional opioids.

Illicit Distribution:

As of May 2020, DEA is aware of 27 new substances that meet the definition of a fentanyl-related substance. Most of these substances were identified in isolated reports. Fifteen substances that meet this definition were first encountered prior to the temporary scheduling action. This demonstrates the effectiveness of the chemical structure-based approach of regulating this class of substances. DEA remains interested in toxicology and harm data and welcomes any reporting connected to fentanyl-related substances.

Control Status:

Fentanyl-related substances, as defined in 21 CFR § 1308.11(h)(30)(i), are controlled in schedule I of the CSA.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; telephone 571-362-3249, or e-mail DPE@usdoj.gov.

¹ <https://www.cdc.gov/mmwr/volumes/67/wr/mm6727a4.htm>
<https://emergency.cdc.gov/han/han00413.asp>

<https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6234a5.htm>
<https://www.cdc.gov/mmwr/volumes/67/wr/mm675152e1.htm>