



**DEPARTMENT OF JUSTICE**

**Drug Enforcement Administration**

**21 CFR Part 1308**

**[Docket No. DEA- 490]**

**Schedules of Controlled Substances: Placement of Furanyl fentanyl, 4-Fluoroisobutyryl fentanyl, Acryl fentanyl, Tetrahydrofuranyl fentanyl, and Ocfentanil in Schedule I**

**AGENCY:** Drug Enforcement Administration, Department of Justice.

**ACTION:** Final order.

**SUMMARY:** With the issuance of this final order, the Acting Administrator of the Drug Enforcement Administration maintains the placement of the substances furanyl fentanyl [*N*-(1-phenethylpiperidin-4-yl)-*N*-phenylfuran-2-carboxamide], 4-fluoroisobutyryl fentanyl or *para*-fluoroisobutyryl fentanyl [*N*-(4-fluorophenyl)-*N*-(1-phenethylpiperidin-4-yl)isobutyramide], acryl fentanyl or acryloylfentanyl [*N*-(1-phenethylpiperidin-4-yl)-*N*-phenylacrylamide], tetrahydrofuranyl fentanyl [*N*-(1-phenethylpiperidin-4-yl)-*N*-phenyltetrahydrofuran-2-carboxamide], and ocfentanil [*N*-(2-fluorophenyl)-2-methoxy-*N*-(1-phenethylpiperidin-4-yl)acetamide], including their isomers, esters, ethers, salts, and salts of isomers, esters and ethers, in schedule I of the Controlled Substances Act. This scheduling action discharges the United States obligations under the Single Convention on Narcotic Drugs (1961). This action continues to impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled

substances on persons who handle (manufacture, distribute, import, export, engage in research or conduct instructional activities with, or possess), or propose to handle, furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil.

**DATES:** Effective [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

**FOR FURTHER INFORMATION CONTACT:** Kathy L. Federico, Regulatory Drafting and Policy Section, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrisette Drive, Springfield, Virginia 22152; Telephone: (202) 598–6812.

**SUPPLEMENTARY INFORMATION:**

**Legal Authority**

Section 201(d)(1) of the Controlled Substances Act (CSA) (21 U.S.C. 811(d)(1)) states that, if control of a substance is required “by United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970, the Attorney General shall issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, without regard to the findings required by [section 201(a) (21 U.S.C. 811(a)] or section [202(b) (21 U.S.C. 812(b)) of the Act] and without regard to the procedures prescribed by [section 201 (a) and (b) (21 U.S.C. 811(a) and (b)].” If a substance is added to one of the schedules of the Single Convention on Narcotic Drugs (1961), then, in accordance with article 3, paragraph 7 of the Convention, as a signatory Member State, the United States is obligated to control the substance under its national drug control legislation, the CSA. The Attorney General has delegated

scheduling authority under 21 U.S.C. 811 to the Administrator of the Drug Enforcement Administration (DEA). 28 CFR 0.100.

## **Background**

On May 15, 2018, the Secretary-General of the United Nations advised the Secretary of State of the United States, that during the 61<sup>st</sup> session of the Commission on Narcotic Drugs, furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil were added to Schedule I of the Single Convention on Narcotic Drugs (1961). This letter was prompted by a decision at the 61<sup>st</sup> session of the Commission on Narcotic Drugs in March 2018 to schedule furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil under Schedule I of the Single Convention on Narcotic Drugs. As a signatory Member State to the Single Convention on Narcotic Drugs, the United States is obligated to control furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil under its national drug control legislation, the CSA, in the schedule deemed most appropriate to carry out its international obligations. 21 U.S.C. 811(d)(1).

## **Furanyl fentanyl, 4-Fluoroisobutyryl fentanyl, Acryl fentanyl, Tetrahydrofuranyl fentanyl, and Ocfentanil**

On November 29, 2016, May 3, 2017, July 14, 2017, October 26, 2017, and February 1, 2018, furanyl fentanyl (81 FR 85873), 4-fluoroisobutyryl fentanyl (82 FR 20544), acryl fentanyl (82 FR 32453), tetrahydrofuranyl fentanyl (82 FR 49504), and ocfentanil (83 FR 4580), respectively, were temporarily placed in schedule I of the CSA upon finding they pose an imminent hazard to the public safety. Furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil share

pharmacological profiles similar to morphine, fentanyl, and other synthetic opioids. Law enforcement and public health reports demonstrate the illicit use and distribution of these substances, which are available on the internet. Furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil are all abused for their opioid-like effects. Evidence suggests the pattern of abuse of these substances parallels that of heroin and prescription opioid analgesics. Because furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil can be obtained through illicit sources, information on their purity and potency are unknown; thus these substances pose a significant adverse health risk to the users.

Similar to morphine and fentanyl, furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil act as  $\mu$ -opioid receptor agonists. Data obtained from preclinical studies (*in vitro* and *in vivo*) demonstrate that furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil produce pharmacological effects similar to fentanyl and morphine. Specifically, in a drug discrimination study in animals, a behavioral test used to determine subjective effects and pharmacological similarity between a test substance and a known drug of abuse, ocfentanil substituted fully for morphine. Additional data obtained from *in vivo* (in animal) studies demonstrated that furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil, similar to fentanyl and morphine, produced an analgesic effect which was attenuated by naltrexone, an opioid receptor antagonist.

Since 2015, furanyl fentanyl has been encountered by law enforcement and public health officials and the adverse health effects and outcomes are demonstrated by fatal

overdose cases. At the time of the temporary scheduling action for furanyl fentanyl in 2016, there were at least 128 confirmed fatalities associated with the misuse and/or abuse of furanyl fentanyl in the United States. According to the National Forensic Laboratory Information System (NFLIS<sup>1</sup>) and STARLiMS<sup>2</sup>, there were 8,516 drug exhibits containing furanyl fentanyl since 2015. For 4-fluoroisobutyryl fentanyl, law enforcement submitted a total of 2,245 drug exhibits since 2016. The DEA has also received reports of at least 62 confirmed fatalities associated with 4-fluoroisobutyryl fentanyl at the time of the temporary order in 2017. NFLIS and STARLiMS reported a total of 2,054 drug exhibits containing acryl fentanyl since 2016. The DEA also received reports of at least 83 confirmed fatalities associated with acryl fentanyl occurring in 2016 and 2017 in the United States. For tetrahydrofuranyl fentanyl, NFLIS and STARLiMS had a total of 23 drug reports since 2015 and there were two confirmed fatalities in the United States at the time of the temporary scheduling action in 2017. There were no reports in NFLIS and STARLiMS for ocfentanil at the time of this final order. However, ocfentanil was first reported in Belgium in 2015 and the exposure resulted in one death; since then, at least two additional deaths in Belgium and Switzerland related to ocfentanil have been reported. It is likely that the prevalence of these substances in opioid-related emergency room admissions and deaths is underreported as standard immunoassays may not differentiate these substances from fentanyl.

The DEA is not aware of any claims or any medical or scientific literature suggesting that furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl

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<sup>1</sup> The National Forensic Laboratory Information System (NFLIS) is a national forensic laboratory reporting system that systematically collects results from drug chemistry analyses conducted by State and local forensic laboratories in the United States. NFLIS data were queried on October 24, 2018. NFLIS is still reporting data for January - July 2018 due to normal lag time in reporting.

<sup>2</sup> STARLiMS is a laboratory information management system that systematically collects results from drug chemistry analyses conducted by DEA laboratories. STARLiMS data were queried on October 24, 2018.

fentanyl, and ocfentanil have a currently accepted medical use in treatment in the United States. In addition, the Department of Health and Human Services (HHS) advised DEA, by letters dated July 8, 2016, January 17, 2017, May 2, 2017, July 14, 2017, and November 8, 2017, that there were no investigational new drug applications or approved new drug applications for furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil, respectively.

The DEA requested that HHS conduct a scientific and medical evaluation and a scheduling recommendation for furanyl fentanyl (by letter dated March 1, 2017), 4-fluoroisobutyryl fentanyl (by letter dated August 28, 2017), acryl fentanyl (by letter dated April 18, 2018), and tetrahydrofuranyl fentanyl (letter dated April 18, 2018). A request for ocfentanil had not previously been submitted. Regardless of these requests and any potential responses from HHS, the DEA is not required under 21 U.S.C. 811(d)(1) to make any findings required by 21 U.S.C. 811(a) or 812(b), and is not required to follow the procedures prescribed by 21 U.S.C. 811(a) and (b). By letter dated June 30, 2018, the Acting Administrator advised HHS that the DEA no longer requires scientific and medical evaluations and scheduling recommendations for furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, as well as, ocfentanil, although not previously requested. The HHS recommendations were no longer required due to the placement of those substances into Schedule I of the Single Convention on Narcotic Drugs (1961) in March 2018. Therefore, consistent with the framework of 21 U.S.C. 811(d), DEA concludes that furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil have no currently accepted medical use in treatment in the United States and are most appropriately placed

(as it has been since May 2017, July 2017, October 2017, November 2017, and February 2018, respectively) in schedule I of the CSA. Further, while the DEA temporarily scheduled these substances under 21 CFR 1308.11(h), a subsection reserved for the temporary listing of substances subject to emergency scheduling, this order moves these substances to 21 CFR 1308.11(b). As explained above, since control is required under the Single Convention on Narcotic Drugs (1961), the DEA will not be initiating regular rulemaking proceedings to schedule these substances pursuant to 21 U.S.C. 811(a).

### **Conclusion**

In order to meet the United States' obligations under the Single Convention on Narcotic Drugs (1961) and because furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil have no currently accepted medical use in treatment in the United States, the Acting Administrator of the Drug Enforcement Administration has determined that these substances should remain in schedule I of the Controlled Substances Act.

### **Requirements for Handling**

Furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil have been controlled as schedule I controlled substances since November 29, 2016, May 3, 2017, July 14, 2017, October 26, 2017, and February 1, 2018, respectively. With publication of this final order, furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil remain subject to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, importation, exportation,

engagement in research, and conduct of instructional activities with, and possession of schedule I controlled substances including the following:

1. *Registration.* Any person who handles (manufactures, distributes, imports, exports, engages in research or conducts instructional activities with, or possesses), or who desires to handle, furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil must be registered with the DEA to conduct such activities pursuant to 21 U.S.C. 822, 823, 957, and 958 and in accordance with 21 CFR parts 1301 and 1312.

2. *Disposal of stocks.* Furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl and ocfentanil must be disposed of in accordance with 21 CFR part 1317, in addition to all other applicable federal, state, local, and tribal laws.

3. *Security.* Furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil are subject to schedule I security requirements and must be handled and stored pursuant to 21 U.S.C. 821, 823, 871(b), and in accordance with 21 CFR 1301.71–1301.93.

4. *Labeling and packaging.* All labels, labeling, and packaging for commercial containers of furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil must be in compliance with 21 U.S.C. 825, 958(e), and be in accordance with 21 CFR part 1302.

5. *Quota.* A quota assigned pursuant to 21 U.S.C. 826 and in accordance with 21 CFR part 1303 is required in order to manufacture furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil.



6. *Inventory.* Every DEA registrant who possesses any quantity of furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil was required to keep an inventory of all stocks of these substances on hand as of November 29, 2016, May 3, 2017, July 14, 2017, October 26, 2017, and February 1, 2018, respectively, pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

7. *Records and Reports.* Every DEA registrant must maintain records and submit reports with respect to furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR parts 1304 and 1312.

8. *Order Forms.* All DEA registrants who distribute furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil must comply with order form requirements pursuant to 21 U.S.C. 828 and in accordance with 21 CFR part 1305.

9. *Importation and Exportation.* All importation and exportation of furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

10. *Liability.* Any activity involving furanyl fentanyl, 4-fluoroisobutyryl fentanyl, acryl fentanyl, tetrahydrofuranyl fentanyl, and ocfentanil not authorized by, or in violation of the CSA, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

## **Regulatory Analyses**

*Executive Order 12866, 13563, and 13771, Regulatory Planning and Review, Improving Regulation and Regulatory Review, and Reducing Regulation and Controlling Regulatory Costs*

This action is not a significant regulatory action as defined by Executive Order 12866 (Regulatory Planning and Review), section 3(f), and the principles reaffirmed in Executive Order 13563 (Improving Regulation and Regulatory Review), and, accordingly, this action has not been reviewed by the Office of Management and Budget (OMB).

This order is not an Executive Order 13771 regulatory action.

*Executive Order 12988, Civil Justice Reform*

This action meets the applicable standards set forth in sections 3(a) and 3(b)(2) of Executive Order 12988 to eliminate drafting errors and ambiguity, minimize litigation, provide a clear legal standard for affected conduct, and promote simplification and burden reduction.

*Executive Order 13132, Federalism*

This action does not have federalism implications warranting the application of Executive Order 13132. This action does not have substantial direct effects on the States, on the relationship between the national government and the States, or on the distribution of power and responsibilities among the various levels of government.

*Executive Order 13175, Consultation and Coordination with Indian Tribal Governments*

This action does not have tribal implications warranting the application of Executive Order 13175. The action does not have substantial direct effects on one or more Indian tribes, on the relationship between the Federal government and Indian tribes, or on the

distribution of power and responsibilities between the Federal government and Indian tribes.

*Administrative Procedure Act*

The CSA provides for an expedited scheduling action where control is required by the United States obligations under international treaties, conventions, or protocols.

21 U.S.C. 811(d)(1). If control is required pursuant to such international treaty, convention, or protocol, the Attorney General must issue an order controlling such drug under the schedule he deems most appropriate to carry out such obligations, without regard to the findings or procedures otherwise required for scheduling actions. *Id.*

To the extent that 21 U.S.C. 811(d)(1) directs that if control is required by the United States obligations under international treaties, conventions, or protocols in effect on October 27, 1970, scheduling actions shall be issued by order (as compared to scheduling pursuant to 21 U.S.C. 811(a) by rule), the DEA believes that the notice and comment requirements of section 553 of the Administrative Procedure Act (APA), 5 U.S.C. 553, do not apply to this scheduling action. In the alternative, even if this action does constitute “rule making” under 5 U.S.C. 551(5), this action is exempt from the notice and comment requirements of 5 U.S.C. 553 pursuant to 21 U.S.C. 553(a)(1) as an action involving a foreign affairs function of the United States given that this action is being done in accordance with 21 U.S.C. 811(d)(1)’s requirement that the United States comply with its obligations under the specified international agreements.

*Regulatory Flexibility Act*

The Regulatory Flexibility Act (RFA) (5 U.S.C. 601–612) applies to rules that are subject to notice and comment under section 553(b) of the APA or any other law. As

explained above, the CSA exempts this final order from notice and comment.

Consequently, the RFA does not apply to this action.

#### *Paperwork Reduction Act of 1995*

This action does not impose a new collection of information requirement under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501–3521. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

#### *Congressional Review Act*

This action is not a major rule as defined by the Congressional Review Act (CRA), 5 U.S.C. 804. This order will not result in: “an annual effect on the economy of \$100,000,000 or more; a major increase in costs or prices for consumers, individual industries, Federal, State, or local government agencies, or geographic regions; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based enterprises to compete with foreign based enterprises in domestic and export markets.” However, pursuant to the CRA, the DEA has submitted a copy of this final order to both Houses of Congress and to the Comptroller General.

#### **List of Subjects in 21 CFR Part 1308**

Administrative practice and procedure, Drug traffic control, Reporting and recordkeeping requirements.

For the reasons set out above, the DEA amends 21 CFR part 1308 as follows:

#### **PART 1308--SCHEDULES OF CONTROLLED SUBSTANCES**

1. The authority citation for part 1308 continues to read as follows:

Authority: 21 U.S.C. 811, 812, 871(b), 956(b), unless otherwise noted.

2. In § 1308.11:

- a. Remove from paragraph (b) introductory text the term “(b)(34)” and add in its place the term “(b)(39)”;
- b. Redesignate paragraphs (b)(57) through (b)(60) as (b)(62) through (b)(65);
- c. Redesignate paragraphs (b)(46) through (b)(56) as (b)(50) through (b)(60);
- d. Redesignate paragraphs (b)(32) through (b)(45) as (b)(35) through (b)(48);
- e. Redesignate paragraphs (b)(4) through (31) as (b)(5) through (32);
- f. Add new paragraphs (b)(4), (b)(33), (b)(34), (b)(49), and (b)(61);
- g. Remove and reserve paragraphs (h)(5), (h)(13), (h)(14), (h)(20), and (h)(29).

The revision and additions to read as follows:

**§ 1308.11 Schedule I.**

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(b) \* \* \*

(4) Acryl fentanyl (*N*-(1-phenethylpiperidin-4-yl)-*N*-phenylacrylamide; other name: acryloylfentanyl).....9811

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(33) 4-Fluoroisobutyryl fentanyl (*N*-(4-fluorophenyl)-*N*-(1-phenethylpiperidin-4-yl)isobutyramide; other name: *para*-fluoroisobutyryl fentanyl) .....9824

(34) Furanyl fentanyl (*N*-(1-phenethylpiperidin-4-yl)-*N*-phenylfuran-2-carboxamide) .....9834

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(49) Ocfentanil (*N*-(2-fluorophenyl)-2-methoxy-*N*-(1-phenethylpiperidin-4-yl)acetamide) .....9838

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(61) Tetrahydrofuranlyl fentanyl (*N*-(1-phenethylpiperidin-4-yl)-*N*-phenyltetrahydrofuran-2-carboxamide).....9843

\* \* \* \* \*

Dated: November 26, 2018

Uttam Dhillon,

Acting Administrator

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