



DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA- 478]

Schedules of Controlled Substances: Placement of Butyryl Fentanyl and U-47700 into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Final order.

SUMMARY: With the issuance of this final order, the Administrator of the Drug Enforcement Administration maintains the placement of the substances butyryl fentanyl (N-(1-phenethylpiperidin-4-yl)-N-phenylbutanamide) and U-47700 (3,4-dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide), 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, butyryl fentanyl and U-47700.

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

FOR FURTHER INFORMATION CONTACT: Michael J. Lewis, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrissette 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) (Administrator). 28 CFR 0.100.

Background

On April 21, 2017, the Secretary-General of the United Nations advised the Secretary of State of the United States, that during the 60th session of the Commission on Narcotic Drugs, butyryl fentanyl and U-47700 were added to schedule I of the Single Convention on Narcotic Drugs, 1961. This letter was prompted by a decision at the 60th session of

the Commission on Narcotic Drugs in March 2017 to schedule butyryl fentanyl and U-47700 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 butyryl fentanyl and U-47700 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).

Butyryl fentanyl and U-47700

On May 12, 2016, and November 14, 2016, butyryl fentanyl and U-47700, respectively, were temporarily placed in schedule I of the CSA by the Administrator in order to avoid an imminent hazard to the public safety ((81 FR 29492- butyryl fentanyl) and (81 FR 79389- U-47700)). Butyryl fentanyl and U-47700 share a pharmacological profile similar to fentanyl, morphine, 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. Both butyryl fentanyl and U-47700 are abused for their opioid-like effects. Evidence suggests the pattern of abuse of butyryl fentanyl and U-47700 parallels that of heroin and prescription opioid analgesics. Because both butyryl fentanyl and U-47700 can be obtained through illicit sources, information on their purity and potency is often unknown, thus posing significant adverse health risks to the users.

Similar to morphine and fentanyl, both butyryl fentanyl and U-47700 act as μ -opioid receptor agonists. Data obtained from preclinical studies (*in vitro* and *in vivo*) demonstrate that butyryl fentanyl and U-47700 produce pharmacological effects similar to fentanyl and morphine. Specifically, in a drug discrimination study in animals, a behavioral test used to determine subjective effect and pharmacological similarity

between a test substance and a known drug of abuse, butyryl fentanyl substituted fully for morphine. Further, data obtained from a drug dependency study showed that butyryl fentanyl completely suppressed signs of withdrawal in morphine-dependent monkeys. Data obtained from *in vivo* (in animal) studies demonstrated that U-47700, similar to fentanyl and morphine, produced analgesic effect and functioned as a μ opioid receptor agonist. Specifically, analgesic activity of U-47700 was attenuated by naltrexone, an opioid receptor antagonist.

Since 2014, butyryl fentanyl has been associated with numerous incidences of adverse health effects in humans. The DEA is aware of at least 40 confirmed fatalities associated with the misuse and/or abuse of butyryl fentanyl in the United States. Similarly, U-47700 has been associated with numerous cases of overdoses and overdose deaths.

The DEA is not aware of any claims or any medical or scientific literature suggesting that butyryl fentanyl and U-47700 have a currently accepted medical use in treatment in the United States. In addition, HHS advised the DEA, by letters dated January 13, 2016, and April 28, 2016, that there were no investigational new drug applications or approved new drug applications for butyryl fentanyl and U-47700.

By letters dated December 8, 2016, and March 1, 2017, the DEA requested that HHS conduct a scientific and medical evaluation of and a scheduling recommendation for butyryl fentanyl and U-47700, respectively. 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 November 1, 2017, the Acting Administrator advised HHS that the DEA no longer

requires scientific and medical evaluations and scheduling recommendations for butyryl fentanyl and U-47700. Therefore, consistent with the framework of 21 U.S.C. 811(d), the DEA concludes that butyryl fentanyl and U-47700 have no currently accepted medical use in treatment in the United States and are most appropriately placed (as they have been since May 2016 and November 2016, 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 both 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 butyryl fentanyl and U-47700 have no currently accepted medical use in treatment in the United States, the Administrator has determined that these substances should remain in schedule I of the CSA.

Requirements for Handling

Butyryl fentanyl and U-47700 have been controlled as schedule I controlled substances since May 12, 2016, and November 14, 2016, respectively. With publication of this final order, butyryl fentanyl and U-47700 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, butyryl fentanyl and U-47700 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.* Butyryl fentanyl and U-47700 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.* Butyryl fentanyl and U-47700 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 butyryl fentanyl and U-47700 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 butyryl fentanyl and U-47700.

6. *Inventory.* Every DEA registrant who possesses any quantity of butyryl fentanyl and U-47700 were required to keep an inventory of all stocks of these substances on hand as of May 12, 2016, and November 14, 2016, 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 butyryl fentanyl and U-47700 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 butyryl fentanyl and U-47700 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 butyryl fentanyl and U-47700 must be in compliance with 21 U.S.C. 952, 953, 957, 958, and in accordance with 21 CFR part 1312.

10. *Liability.* Any activity involving butyryl fentanyl and U-47700 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

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

Executive Order 13132

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

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 section 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act (CRA)). 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. Redesignate paragraphs (b)(18) through (58) as (b)(19) through (59) and add a new paragraph (b)(18);

b. Add paragraph (b)(60); and

c. Remove and reserve paragraphs (h)(2) and (4).

The additions read as follows:

§ 1308.11 Schedule I.

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(b) * * *

(18) Butyryl fentanyl (N-(1-phenethylpiperidin-4-yl)-N-phenylbutyramide).....9822

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(60) U-47700 (3,4-Dichloro-N-[2-(dimethylamino)cyclohexyl]-N-methylbenzamide).....9547

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Dated: April 11, 2018.

Robert W. Patterson,

Acting Administrator.

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