



**DEPARTMENT OF JUSTICE**

**Drug Enforcement Administration**

**21 CFR Part 1308**

**[Docket No. DEA-715]**

**Schedules of Controlled Substances: Placement of Oliceridine in Schedule II**

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

**ACTION:** Interim final rule, with request for comments.

**SUMMARY:** On August 7, 2020, the U.S. Food and Drug Administration approved a new drug application for oliceridine, chemically known as *N*-[(3-methoxythiophen-2-yl)methyl] (2-[(9*R*)-9-(pyridin-2-yl)-6-oxaspiro[4.5]decan-9-yl]ethyl)amine fumarate. The Department of Health and Human Services provided the Drug Enforcement Administration (DEA) with a scheduling recommendation to place oliceridine in schedule II of the Controlled Substances Act (CSA). In accordance with the CSA, as revised by the Improving Regulatory Transparency for New Medical Therapies Act, DEA is hereby issuing an interim final rule placing oliceridine, including its isomers, esters, ethers, salts and salts of isomers, esters and ethers whenever the existence of such isomers, esters, ethers and salts is possible, in schedule II of the CSA.

**DATES:** The effective date of this rulemaking is [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER]. Interested persons may file written comments on this rulemaking in accordance with 21 U.S.C. 811(j)(3) and 21 CFR 1308.43(g). Electronic

comments must be submitted, and written comments must be postmarked, on or before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER]. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after 11:59 p.m. Eastern Time on the last day of the comment period.

Interested persons may file a request for hearing or waiver of hearing in accordance with 21 U.S.C. 811(j)(3) and 21 CFR 1308.44. Requests for hearing and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

**ADDRESSES:** To ensure proper handling of comments, please reference “Docket No. DEA-715” on all correspondence, including any attachments.

- *Electronic comments:* The Drug Enforcement Administration encourages that all comments be submitted electronically through the Federal eRulemaking Portal, which provides the ability to type short comments directly into the comment field on the Web page or attach a file for lengthier comments. Please go to <http://www.regulations.gov> and follow the online instructions at that site for submitting comments. Upon completion of your submission, you will receive a Comment Tracking Number for your comment. Please be aware that submitted comments are not instantaneously available for public view on Regulations.gov. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment.

- *Paper comments:* Paper comments that duplicate the electronic submission are not necessary and are discouraged. Should you wish to mail a paper comment *in lieu of* an electronic comment, it should be sent via regular or express mail to: Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrisette Drive, Springfield, VA 22152.

- *Hearing requests:* All requests for hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrisette Drive, Springfield, Virginia 22152. All requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/LJ, 8701 Morrisette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrisette Drive, Springfield, Virginia 22152.

**FOR FURTHER INFORMATION CONTACT:** Scott A. Brinks, Regulatory Drafting and Policy Support Section, Diversion Control Division, Drug Enforcement Administration; Mailing Address: 8701 Morrisette Drive, Springfield, Virginia 22152; Telephone: (571) 362-3261.

**SUPPLEMENTARY INFORMATION:**

**Posting of Public Comments**

Please note that all comments received are considered part of the public record. They will, unless reasonable cause is given, be made available by the Drug Enforcement Administration (DEA) for public inspection online at <http://www.regulations.gov>. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter. The Freedom of Information Act applies to all

comments received. If you want to submit personal identifying information (such as your name, address, etc.) as part of your comment, but do not want it to be made publicly available, you must include the phrase “PERSONAL IDENTIFYING INFORMATION” in the first paragraph of your comment. You must also place all of the personal identifying information you do not want made publicly available in the first paragraph of your comment and identify what information you want redacted.

If you want to submit confidential business information as part of your comment, but do not want it to be made publicly available, you must include the phrase “CONFIDENTIAL BUSINESS INFORMATION” in the first paragraph of your comment. You must also prominently identify the confidential business information to be redacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will generally be made publicly available in redacted form. If a comment has so much confidential business information or personal identifying information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments posted to <http://www.regulations.gov> may include any personal identifying information (such as name, address, and phone number) included in the text of your electronic submission that is not identified as directed above as confidential.

An electronic copy of this document and supplemental information, including the complete Department of Health and Human Services (HHS) and DEA eight-factor analyses, to this interim final rule (IFR) are available at <http://www.regulations.gov> for easy reference.

## **Request for Hearing or Appearance; Waiver**

Pursuant to 21 U.S.C. 811(a), this action is a formal rulemaking “on the record after opportunity for a hearing.” Such proceedings are conducted pursuant to the provisions of the Administrative Procedure Act (APA), 5 U.S.C. 551–559. 21 CFR 1308.41–1308.45; 21 CFR part 1316, subpart D. Interested persons may file requests for a hearing or notices of intent to participate in a hearing in conformity with the requirements of 21 CFR 1308.44 (a) or (b), and include a statement of interest in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any interested person may file a waiver of an opportunity for a hearing or to participate in a hearing together with a written statement regarding the interested person’s position on the matters of fact and law involved in any hearing as set forth in 21 CFR 1308.44(c).

All requests for a hearing and waivers of participation must be sent to DEA using the address information provided above.

## **Background and Legal Authority**

Under the Improving Regulatory Transparency for New Medical Therapies Act, Public Law 114-89, § 2(b), 129 Stat. 698, 700 (2015), DEA is required to commence an expedited scheduling action with respect to certain new drugs approved by the U.S. Food and Drug Administration (FDA). As provided in 21 U.S.C. 811(j), this expedited scheduling is required where both of the following conditions apply: (1) The Secretary of the Department of Health and Human Services (the Secretary) has advised DEA that an application for a new drug has been submitted for a drug that has a stimulant, depressant, or hallucinogenic effect on the central nervous system, and that it appears that such drug

has an abuse potential; and, (2) the Secretary recommends that DEA control the drug in schedule II, III, IV, or V pursuant to 21 U.S.C. 811(a) and (b). In these circumstances, DEA is required to issue an IFR controlling the drug within 90 days.

The law further states that the 90-day timeframe starts the later of (1) the date DEA receives the HHS scientific and medical evaluation/scheduling recommendation, or (2) the date DEA receives notice of the application approval by HHS. In addition, the law specifies that the rulemaking shall become immediately effective as an IFR without requiring DEA to demonstrate good cause therefor. Thus, the purpose of subsection (j) is to speed the process by which DEA schedules newly approved drugs that are currently either in schedule I or not controlled (but which have sufficient abuse potential to warrant control) so that such drugs may be marketed without undue delay following FDA approval.<sup>1</sup>

Subsection (j) further provides that the IFR shall give interested persons the opportunity to comment and to request a hearing. After the conclusion of such proceedings, DEA must issue a final rule in accordance with the scheduling criteria of subsections 21 U.S.C. 811(b), (c), and (d) and 21 U.S.C. 812(b).

On November 2, 2017, Trevena, Inc. (Sponsor) submitted an initial New Drug Application (NDA) to FDA for oliceridine that was subsequently resubmitted on February 7, 2020. FDA determined that oliceridine is a new molecular entity, and HHS determined that oliceridine has a depressant effect on the central nervous system. On August 7, 2020, FDA approved the NDA for oliceridine for medical use as an

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<sup>1</sup> Given the parameters of subsection (j), in DEA's view, it would not apply to a reformulation of a drug containing a substance currently in schedules II through V for which an NDA has recently been approved.

intravenous drug for the management of acute pain severe enough to require an intravenous opioid analgesic and for patients for whom alternative treatments are inadequate.

### **Determination to Schedule Oliceridine**

On July 27, 2020, DEA received a scientific and medical evaluation document from HHS prepared by FDA related to oliceridine, titled: “Basis for the Recommendation to Control Oliceridine and its Salts in Schedule II of the Controlled Substances Act.” Pursuant to 21 U.S.C. 811(b), this document contained an eight-factor analysis of the abuse potential of oliceridine, along with HHS’s recommendation to control oliceridine under schedule II of the CSA. Subsequently, on August 7, 2020, DEA received notification from HHS that FDA had approved an NDA for oliceridine (OLINVYK).

In response, DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by HHS, along with all other relevant data, and completed its own eight-factor review document pursuant to 21 U.S.C. 811(c). DEA concluded that oliceridine met the 21 U.S.C. 812(b)(2) criteria for placement in schedule II of the CSA.

Pursuant to subsection 811(j), and based on HHS’s recommendation, the NDA approval by HHS/FDA, and DEA’s determination, DEA is issuing this IFR to schedule oliceridine as a schedule II controlled substance under the CSA.

Included below is a brief summary of each factor as analyzed by HHS and DEA, and as considered by DEA in its scheduling action. Please note that both the DEA and HHS analyses are available in their entirety under “Supporting Documents” in the public docket for this IFR at <http://www.regulations.gov>, under Docket Number “DEA-715.”

Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. *Its Actual or Relative Potential for Abuse:* Oliceridine is a new molecular entity that has not been marketed in the United States or any other country. Thus, information about the diversion and actual abuse of oliceridine is limited. Oliceridine is currently not available for medical treatment, has not been diverted from legitimate sources, and individuals have not taken this substance in amounts sufficient to create a hazard to public health and safety. DEA notes that there are no reports for oliceridine in the National Forensic Laboratory Information System (NFLIS),<sup>2</sup> which collects drug identification results from drug cases submitted to and analyzed by Federal, State, and local forensic laboratories. There were also no reports in DEA's laboratory drug evidence data system of record, STARLiMS.<sup>3</sup>

According to the legislative history of the CSA, one of the criteria by which DEA should assess actual or relative potential for abuse is whether the substance in question "is so related in its action to a substance already listed as having a potential for abuse to make it likely that it will have the same potential for abuse as such substance, thus making it reasonable to assume that there may be significant diversions from legitimate

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<sup>2</sup> NFLIS represents an important resource in monitoring illicit drug trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS is a comprehensive information system that includes data from forensic laboratories that handle more than 96 percent of an estimated 1.0 million distinct annual State and local drug analysis cases. NFLIS includes drug chemistry results from completed analyses only. While NFLIS data is not direct evidence of abuse, it can lead to an inference that a drug has been diverted and abused. *See* 76 FR 77330, 77332 (Dec. 12, 2011). NFLIS data were queried on July 28, 2020.

<sup>3</sup> On October 1, 2014, DEA implemented STARLiMS (a web-based, commercial laboratory information management system) to replace the System to Retrieve Information from Drug Evidence (STRIDE) as its laboratory drug evidence data system of record. DEA laboratory data submitted after September 30, 2014, are reposted in STARLiMS. STARLiMS data were queried on July 28, 2020.

channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.”<sup>4</sup> As stated by HHS, oliceridine is a high-affinity mu opioid agonist that produces behavioral effects similar to other mu opioid agonists, such as the schedule II opioid morphine. Moreover, in a rat drug discrimination study, oliceridine generalized to morphine, showing that oliceridine has opioid-like properties. In a clinical study investigating the abuse potential of oliceridine, HHS concluded that oliceridine produced subjective responses that were similar to those for morphine. Specifically, like morphine, oliceridine produced positive subjective responses and euphoria-related adverse events in clinical studies. Together, this evidence demonstrates that oliceridine is related in action and effect to the schedule II substance morphine, and can therefore be expected to have a similar potential for abuse.

2. *Scientific Evidence of Its Pharmacological Effects, if Known:* Oliceridine has high affinity for the mu-opioid receptor and does not bind to any other receptors that are typically associated with abuse, such as kappa and delta opioid receptors, cannabinoid receptors, GABAergic receptors, or other ion channels. According to HHS, general behavioral studies in animals indicate that oliceridine produces behavioral and motor effects similar to those of morphine, a schedule II substance. Additionally, oliceridine produces self-administration in rats. Furthermore, in a drug discrimination study used to predict subjective effects in humans, oliceridine mimicked the stimulus effects of morphine. In a human abuse potential (HAP) study, therapeutic and supratherapeutic

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<sup>4</sup> Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91-1444, 91st Cong., Sess. 1 (1970), reprinted in U.S.C.C.A.N. 4566, 4603.

doses of oliceridine produced euphoria, somnolence, and paresthesia. These adverse events are consistent with those of other schedule II opioids such as morphine. In other clinical studies, adverse events such as somnolence, sedation, anxiety, restlessness, and paresthesia were seen in subjects treated with oliceridine. As concluded by HHS, results from preclinical and clinical studies indicate that oliceridine has abuse potential similar to morphine.

3. *The State of Current Scientific Knowledge Regarding the Drug or Other*

*Substance:* Oliceridine is a new molecular entity, chemically known as *N*-[(3-methoxythiophen-2-yl)methyl] (2-[(9*R*)-9-(pyridin-2-yl)-6-oxaspiro [4.5]decan-9-yl]ethyl)amine fumarate. It has a molecular formula of  $C_{22}H_{30}N_2O_2S.C_4H_4O_4$ . Oliceridine is a white to lightly-colored solid that is sparingly soluble in water. On August 7, 2020, FDA approved an NDA for oliceridine for medical use to manage acute pain severe enough to require an intravenous opioid analgesic and for which alternative treatments are inadequate. Thus, oliceridine has an accepted medical use in the United States. Oliceridine will be marketed as an intravenous medication formulated in vials containing 1, 2, or 30 mg of oliceridine.

4. *Its History and Current Pattern of Abuse:* There is no information available relating to the history and current pattern of abuse of oliceridine, since this drug is not currently marketed in any country. HHS notes that oliceridine produces abuse-related signals, such as euphoria and somnolence, and abuse potential similar to that of schedule II controlled substance morphine. DEA searched NFLIS and STARLiMS databases for oliceridine encounters. Consistent with the fact that oliceridine is a new molecular entity, these databases had no records of encounters of oliceridine by law enforcement.

5. *The Scope, Duration, and Significance of Abuse:* Oliceridine is currently not marketed in any country. Thus, information on the scope, duration, and significance of abuse for oliceridine is lacking. However, as stated by HHS, data from animal and human studies indicate that oliceridine has abuse potential similar to morphine. Therefore, upon marketing, oliceridine scope of abuse is expected to be similar to morphine.

6. *What, if any, Risk There is to the Public Health:* The extent of abuse potential of a drug is an indication of its public health risk. Data from the preclinical and clinical studies suggest that the abuse potential and physical or psychological dependence potential of oliceridine are similar to the schedule II substance morphine. Thus, oliceridine upon its availability for marketing would be expected to create a public health risk.

7. *Its Psychic or Physiological Dependence Liability:* Physical dependence for oliceridine was tested in an animal toxicity study. According to HHS, the animal toxicity study using rats demonstrated dose-dependent decreases in food consumption and body weight as well as classic opioid withdrawal signs from discontinuation of oliceridine. In a rat self-administration study as well as in clinical studies, oliceridine produced rewarding effects similar to morphine. Based on these studies, HHS stated that oliceridine may produce physical and psychological dependence.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled under the CSA:* Oliceridine is not an immediate precursor of any controlled substance, as defined in 21 U.S.C. 802(23).

*Conclusion:* After considering the scientific and medical evaluation conducted by HHS, HHS's scheduling recommendation, and its own eight-factor analysis, DEA has determined that these facts and all relevant data constitute substantial evidence of a potential for abuse of oliceridine. As such, DEA hereby schedules oliceridine as a controlled substance under the CSA.

### **Determination of Appropriate Schedule**

The CSA outlines the findings required to place a drug or other substance in any particular schedule (I, II, III, IV, or V). 21 U.S.C. 812(b). After consideration of the analysis and recommendation of the Assistant Secretary for Health of HHS and review of all available data, the Acting Administrator of DEA, pursuant to 21 U.S.C. 812(b)(2), finds that:

#### **1. Oliceridine has a high potential for abuse**

Oliceridine is a mu-opioid receptor agonist and produces behavioral effects that are similar to those of morphine (schedule II opioid substance) in animals and humans. A self-administration study in animals demonstrated that oliceridine produced self-administration that was comparable to morphine. Additionally, a drug-discrimination study in animals demonstrated that oliceridine generalized to morphine, indicating that it has mu-opioid receptor agonist properties. Results from a HAP study showed that oliceridine produces positive subjective effects as well as adverse events such as euphoria, similar to that of morphine, a schedule II substance with a high potential for abuse. Lastly, clinical studies in healthy individuals indicate that oliceridine produces abuse-related adverse events such as euphoria and sedation. These data collectively

indicate that oliceridine has a high potential for abuse similar to the schedule II substance morphine.

**2. Oliceridine has a currently accepted medical use in the United States.**

FDA recently approved a NDA for oliceridine for the management of acute pain severe enough to require an intravenous opioid analgesic and for patients for whom alternative treatments are inadequate. Thus, oliceridine has a currently accepted medical use in treatment in the United States.

**3. Abuse of oliceridine may lead to severe psychological or physical dependence**

Chronic administration of oliceridine in rats followed by drug discontinuation produced classic opioid withdrawal signs, similar to that of schedule II drug morphine. This study would indicate oliceridine's potential to cause physical dependence similar to that of morphine. Oliceridine also produces self-administration in rats and positive subjective responses in a HAP study. These results parallel those produced by morphine and suggest that oliceridine can also produce psychological dependence. These data collectively suggest that oliceridine abuse may lead to psychological and physical dependence similar to that of schedule II opioids.

Based on these findings, the Acting Administrator of DEA concludes that oliceridine warrants control in schedule II of the CSA. 21 U.S.C. 812(b)(2).

**Requirements for Handling Oliceridine**

Oliceridine is subject to the CSA's schedule II regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, importing, exporting, research, and conduct of

instructional activities and chemical analysis with, and possession involving schedule II substances, including the following:

1. *Registration.* Any person who handles (manufactures, distributes, reverse distributes, dispenses, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses) oliceridine, or who desires to handle oliceridine, must be registered with 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. Any person who currently handles or intends to handle oliceridine, and is not registered with DEA, must submit an application for registration and may not continue to handle oliceridine, unless DEA has approved the application for registration, pursuant to 21 U.S.C. 822, 823, 957, and 958, and in accordance with 21 CFR parts 1301 and 1312.

2. *Quota.* Only registered manufacturers are permitted to manufacture oliceridine in accordance with a quota assigned pursuant to 21 U.S.C. 826 and in accordance with 21 CFR part 1303.

3. *Disposal of stocks.* Any person who does not desire or is not able to maintain a schedule II registration must surrender all quantities of currently held oliceridine, or may transfer all quantities of currently held oliceridine to a person registered with DEA in accordance with 21 CFR part 1317, in addition to all other applicable Federal, State, local, and tribal laws.

4. *Security.* Oliceridine is subject to schedule II security requirements and must be handled and stored pursuant to 21 U.S.C. 821 and 823 and in accordance with 21 CFR 1301.71–1301.93.

5. *Labeling and Packaging.* All labels, labeling, and packaging for commercial containers of oliceridine must comply with 21 U.S.C. 825 and 958(e) and be in accordance with 21 CFR part 1302.

6. *Inventory.* Every DEA registrant who possesses any quantity of oliceridine must take an inventory of oliceridine on hand, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

Any person who becomes registered with DEA to handle oliceridine must take an initial inventory of all stocks of controlled substances containing oliceridine on hand on the date the registrant first engages in the handling of controlled substances, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

After the initial inventory, every DEA registrant must take a new inventory of all stocks of controlled substances (including oliceridine) on hand every two years, pursuant to 21 U.S.C. 827 and 958(e), 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 for oliceridine, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR parts 1304, 1312, and 1317.

8. *Orders for oliceridine.* Every DEA registrant who distributes oliceridine is required to comply with order form requirements, pursuant to 21 U.S.C. 828, and in accordance with 21 CFR part 1305.

9. *Prescriptions.* All prescriptions for oliceridine or products containing oliceridine must comply with 21 U.S.C. 829, and be issued in accordance with 21 CFR parts 1306 and 1311, subpart C.

10. *Manufacturing and Distributing.* In addition to the general requirements of the CSA and DEA regulations that are applicable to manufacturers and distributors of schedule II controlled substances, such registrants should be advised that (consistent with the foregoing considerations) any manufacturing or distribution of oliceridine may only be for the legitimate purposes consistent with the drug's labeling, or for research activities authorized by the Federal Food, Drug, and Cosmetic Act, as applicable, and the CSA.

11. *Importation and Exportation.* All importation and exportation of oliceridine must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

12. *Liability.* Any activity involving oliceridine not authorized by, or in violation of, the CSA or its implementing regulations, is unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

## **Regulatory Analyses**

### *Administrative Procedure Act*

Public Law 114-89 was signed into law, amending 21 U.S.C. 811. This amendment provides that in cases where a new drug is (1) approved by HHS, and (2) HHS recommends control in CSA schedule II–V, DEA shall issue an IFR scheduling the drug within 90 days. Additionally, the law specifies that the rulemaking shall become immediately effective as an IFR without requiring DEA to demonstrate good cause.

Therefore, DEA has determined that the notice and comment requirements of section 553 of the APA, 5 U.S.C. 553, do not apply to this scheduling action.

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

In accordance with 21 U.S.C. 811(a) and (j), this scheduling action is subject to formal rulemaking procedures performed “on the record after opportunity for a hearing,” which are conducted pursuant to the provisions of 5 U.S.C. 556 and 557. The CSA sets forth the procedures and criteria for scheduling a drug or other substance. Such actions are exempt from review by the Office of Management and Budget (OMB) pursuant to section 3(d)(1) of Executive Order (E.O.) 12866 and the principles reaffirmed in E.O. 13563.

This IFR is not an E.O. 13771 regulatory action pursuant to E.O. 12866 and OMB guidance.<sup>5</sup>

*Executive Order 12988, Civil Justice Reform*

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

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<sup>5</sup> Office of Management and Budget, Executive Office of The President, Interim Guidance Implementing Section 2 of the Executive Order of January 30, 2017, Titled “Reducing Regulation and Controlling Regulatory Costs” (Feb. 2, 2017).

*Executive Order 13132, Federalism*

This rulemaking does not have federalism implications warranting the application of E.O. 13132. The rule 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 rule does not have tribal implications warranting the application of E.O. 13175. It 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.

*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. Under 21 U.S.C. 811(j), DEA is not required to publish a general notice of proposed rulemaking. Consequently, the RFA does not apply to this IFR.

*Unfunded Mandates Reform Act of 1995*

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 *et seq.*, DEA has determined that this action would not result in any Federal mandate that may result “in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million or more (adjusted for inflation) in any one year.” Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

*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. This action does not impose recordkeeping or reporting requirements on State or local governments, individuals, businesses, or organizations. 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 rule is not a major rule as defined by the Congressional Review Act (CRA), 5 U.S.C. 804. This rule does not result in: an annual effect on the economy of \$100 million 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 U.S.-based companies to compete with foreign based companies in domestic and export markets. However, pursuant to the CRA, DEA has submitted a copy of this IFR to both Houses of Congress and to the Comptroller General.

**List of Subjects**

**21 CFR Part 1308**

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

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

**PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES**

1. The authority citation for 21 CFR part 1308 continues to read as follows:

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

2. Amend § 1308.12 by:

- a. Redesignating paragraph (c)(18) through (c)(29) as (c)(19) through (c)(30);
- b. Adding new paragraph (c)(18).

The addition to read as follows:

**§ 1308.12 Schedule II.**

\* \* \* \* \*

(c) \* \* \*

(18) Oliceridine (*N*-[(3-methoxythiophen-2-yl)methyl]({2-[(9*R*)-9-(pyridin-2-yl)-6-oxaspiro [4.5]decan-9-yl]ethyl})amine fumarate)..... 9245

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**Timothy J. Shea,**  
*Acting Administrator*

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