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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA-484]

Schedules of Controlled Substances: Placement of beta-Hydroxythiofentanyl into Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration proposes placing beta-hydroxythiofentanyl (*N*-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-*N*-phenylpropionamide) also known as N-[1-[2-hydroxy-2-(2-thienyl)ethyl]4-piperidinyl]N-phenyl-propanamide including its isomers, esters, ethers, salts, and salts of isomers, esters and ethers, in schedule I of the Controlled Substances Act. If finalized, this action would 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, conduct instructional activities or chemical analysis, or possess), or propose to handle beta-hydroxythiofentanyl.

DATES: Comments must be submitted electronically or postmarked on or before [INSERT DATE 30 DAYS AFTER PUBLICATION IN THE FEDERAL REGISTER].

Interested persons may file a request for hearing or waiver of hearing pursuant to 21 CFR 1308.44 and in accordance with 21 CFR 1316.45 and/or 1316.47, as applicable.

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: Interested persons may file written comments on this proposal in accordance with 21 CFR 1308.43(g). 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. To ensure proper handling of comments, please reference "Docket No. DEA-484" on all electronic and written 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 to 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. 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/DRW, 8701 Morrissette Drive, Springfield, Virginia 22152.

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

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:

Posting of Public Comments

Please note that all comments received in response to this docket 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 (FOIA) 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 confidential business information to be redacted within the comment.

Comments containing personal identifying information and confidential business information identified as directed above will 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 to this proposed rule are available at *http://www.regulations.gov* for easy reference.

Request for Hearing or Waiver of Participation in a Hearing

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. Such requests or notices must conform to the

requirements of 21 CFR 1308.44 (a) or (b), and 1316.47 or 1316.48, as applicable, and include a statement of the person's interests in the proposed scheduling action, whether the person is adversely affected or aggrieved, and the objections or issues, if any, concerning which the person desires to be heard at a hearing. Any waiver must conform to the requirements of 21 CFR 1308.44(c) and may include a written statement regarding the interested person's position on the matters of fact and law involved in any hearing.

Please note that pursuant to 21 U.S.C. 811(a), the purpose and subject matter of a hearing held in relation to this rulemaking are restricted to: "(A) find[ing] that such drug or other substance has a potential for abuse, and (B) mak[ing] with respect to such drug or other substance the findings prescribed by subsection (b) of section 812 of this title for the schedule in which such drug is to be placed * * *." All requests for hearing and waivers of participation must be sent to the DEA using the address information provided above.

Legal Authority

The Controlled Substances Act (CSA) provides that proceedings for the issuance, amendment, or repeal of the scheduling of any drug or other substance may be initiated by the Attorney General (1) on his own motion; (2) at the request of the Secretary of the Department of Health and Human Services (HHS),[1] or (3) on the petition of any interested party. 21 U.S.C. 811(a). This proposed action is supported by a recommendation from the Assistant Secretary for Health of the HHS (Assistant

[1] As discussed in a memorandum of understanding entered into by the Food and Drug Administration (FDA) and the National Institute on Drug Abuse (NIDA), the FDA acts as the lead agency within the HHS in carrying out the Secretary's scheduling responsibilities under the CSA, with the concurrence of NIDA. 50 FR 9518, Mar. 8, 1985. The Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations. 58 FR 35460, July 1, 1993.

Secretary) and an evaluation of all other relevant data by the DEA. If finalized, this action would continue[2] to impose the regulatory controls and administrative, civil, and criminal sanctions of schedule I controlled substances on any person who handles or proposes to handle beta-hydroxythiofentanyl.

Background

On May 12, 2016, the DEA published a final order in the *Federal Register* amending 21 CFR 1308.11(h) to temporarily place beta-hydroxythiofentanyl (*N*-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-*N*phenylpropionamide in schedule I of the CSA pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). 81 FR 29492. That temporary scheduling order was effective on the date of publication, and was based on findings by the Acting Administrator of the DEA (Acting Administrator) that the temporary scheduling of beta-hydroxythiofentanyl was necessary to avoid an imminent hazard to public safety pursuant to 21 U.S.C. 811(h)(1). Section 201(h)(2) of the CSA, 21 U.S.C. 811(h)(2), requires that the temporary control of this substance expire two years from the effective date of the scheduling order, which was May 12, 2016. However, the CSA also provides that during the pendency of proceedings under 21 U.S.C. 811(a)(1) with respect to the substance, the temporary scheduling of that substance could be extended for up to one year. Proceedings for the scheduling of a substance under 21 U.S.C. 811(a) may be initiated by the Attorney General (delegated to the Administrator of the DEA pursuant to 28 CFR 0.100) on his own motion, at the request of the Secretary

[2] beta-Hydroxythiofentanyl is currently subject to schedule I controls on a temporary basis, pursuant to 21 U.S.C. 811(b). 81 FR 29492, May 12, 2016.

of HHS[3], or on the petition of any interested party. An extension of the existing temporary order is being ordered by the Acting Administrator in a separate action, and is published elsewhere in this issue of the *Federal Register*.

The Acting Administrator, on his own motion pursuant to 21 U.S.C. 811(a), is initiating proceedings under 21 U.S.C. 811(a)(1) to permanently schedule beta-hydroxythiofentanyl. The DEA has gathered and reviewed the available information regarding the pharmacology, chemistry, trafficking, actual abuse, pattern of abuse, and the relative potential for abuse for beta-hydroxythiofentanyl. On December 8, 2016, the Acting Administrator submitted a request to the Assistant Secretary to provide the DEA with a scientific and medical evaluation of available information and a scheduling recommendation for butyryl fentanyl and beta-hydroxythiofentanyl, in accordance with 21 U.S.C. 811(b) and (c). In a letter dated November 1, 2017, DEA notified HHS that it no longer required a scientific and medical evaluation for butyryl fentanyl because the Commission on Narcotic Drugs (CND), at its 60th session, added butyryl fentanyl to Schedule I of the Single Convention on Narcotic Drugs, 1961. On April 20, 2018, the DEA published a final scheduling order for butyryl fentanyl (83 FR 17486) to meet international treaty obligations pursuant to 21 U.S.C. 811(d)(1).

Upon evaluating the scientific and medical evidence, on April 27, 2018, the Assistant Secretary submitted to the Acting Administrator HHS's scientific and medical evaluation and scheduling recommendation for beta-hydroxythiofentanyl. Upon receipt of the scientific and medical evaluation and scheduling recommendation from the HHS, the

[3] Because the Secretary of HHS has delegated to the Assistant Secretary the authority to make domestic drug scheduling recommendations, for purposes of this proposed rulemaking, all subsequent references to "Secretary" have been replaced with "Assistant Secretary."

DEA reviewed the documents and all other relevant data, and conducted its own eight-factor analysis of the abuse potential of beta-hydroxythiofentanyl in accordance with 21 U.S.C. 811(c).

Proposed Determination to Schedule beta-Hydroxythiofentanyl

As discussed in the background section, the Acting Administrator is initiating proceedings, pursuant to 21 U.S.C. 811(a)(1), to add beta-hydroxythiofentanyl permanently to schedule I. The DEA has reviewed the scientific and medical evaluations and scheduling recommendation, received from HHS, and all other relevant data and conducted its own eight-factor analysis of the abuse potential of beta-hydroxythiofentanyl pursuant to 21 U.S.C. 811(c). Included below is a brief summary of each factor as analyzed by the HHS and the DEA, and as considered by the DEA in its proposed scheduling action. Please note that both the DEA 8-Factor and HHS 8-Factor analyses and the Assistant Secretary's April 27, 2018, letter, are available in their entirety under the tab "Supporting Documents" of the public docket for this action at *http://www.regulations.gov* under Docket Number "DEA-484."

1. *The Drug's Actual or Relative Potential for Abuse*: The term "abuse" is not defined in the CSA. However, the legislative history of the CSA suggests that the DEA consider the following criteria when determining whether a particular drug or substance has a potential for abuse[4]:

> *a) There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or of the community; or*

[4] COMPREHENSIVE DRUG ABUSE PREVENTION AND CONTROL ACT OF 1970, H.R. REP. NO. 91-1444, 91st Cong., Sess. 1 (1970); *reprinted in* 1970 U.S.C.C.A.N. 4566, 4603.

b) There is significant diversion of the drug or drugs containing such a substance from legitimate drug channels; or

c) Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice; or

d) The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate 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.

The abuse potential of beta-hydroxythiofentanyl is associated with its pharmacological similarity to other schedule I and II mu-opioid receptor agonist substances which have a high potential for abuse. Similar to morphine, fentanyl and several schedule I opioid substances that are structurally related to fentanyl, beta-hydroxythiofentanyl has been shown to bind and act as a μ -opioid receptor agonist.

beta-Hydroxythiofentanyl has no approved medical use in the United States and has been encountered on the illicit drug market. The use of beta-hydroxythiofentanyl has been associated with adverse outcomes to include death. Because beta-hydroxythiofentanyl is not an approved drug product, a practitioner may not legally prescribe it, and this substance cannot be dispensed to an individual. Therefore, the use of beta-hydroxythiofentanyl is without medical advice, and accordingly, leads to the conclusion that beta-hydroxythiofentanyl is abused for its opioidergic properties. There are no legitimate drug channels for beta-hydroxythiofentanyl as a marketed drug product but it's available for purchase from legitimate chemical companies because it is used in

scientific research. However, despite the limited legitimate use of this substance, reports from public health and law enforcement communicate that beta-hydroxythiofentanyl is being abused and taken in amounts sufficient to create a hazard to an individual's health. This is evidenced by the positive toxicological identification of beta-hydroxythiofentanyl in several (n = 25) overdose deaths. Data from forensic databases can be used as an indicator of illicit activity with drugs and abuse[5] within the United States. According to the National Forensic Laboratory Information System (NFLIS)[6] which collects and analyzes drug exhibits submitted to Federal, State and Local forensic laboratories, there were ten reports (from Florida) of beta-hydroxythiofentanyl within this database in 2015. Consequently, the positive identification of beta-hydroxythiofentanyl in law enforcement encounters and toxicological screenings of overdose deaths indicates that this substance is being abused, and thus poses safety hazards to the health of users.

2. *Scientific Evidence of the Drug's Pharmacological Effects, if Known*: beta-Hydroxythiofentanyl is pharmacologically similar to other schedule I and schedule II mu-opioid receptor agonist substances. The abuse potential (assessed by drug discriminative study and self-administration study) of beta-hydroxythiofentanyl has not been studied in non-clinical or clinical studies, however the non-clinical and clinical studies conducted on abuse potential of mu-opioid receptor agonists such as morphine and fentanyl indicate that these drugs share discriminative stimulus effects and that these drugs have reinforcing properties. Similar to schedule I and II opioid analgesics, beta-

5 While law enforcement 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.

6 NFLIS is a DEA program and 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. The NFLIS database also contains Federal data from U.S. Customs and Border Protection (CBP). NFLIS only includes drug chemistry results from completed analyses.

hydroxythiofentanyl binds to and activates the mu-opioid receptor. Additionally, behavioral studies in animals demonstrate that similar to fentanyl and morphine, beta-hydroxythiofentanyl produces analgesic effect. Pre-treatment with naltrexone, an opioid antagonist, attenuated analgesic effects of beta-hydroxythiofentanyl, fentanyl and morphine. These data indicate that beta-hydroxythiofentanyl is a CNS active mu-opioid receptor agonist that is about 10 times more potent than morphine. Thus, it is concluded from *in vitro* and *in vivo* pharmacological studies that effects of beta-hydroxythiofentanyl are similar to that of fentanyl and morphine and is mediated by mu-opioid receptor agonism.

3. *The State of Current Scientific Knowledge Regarding the Drug or Other Substance*: beta-Hydroxythiofentanyl is a synthetic opioid of the 4-anilidopiperidine structural class which includes fentanyl and thiofentanyl. The chemical structure of beta-hydroxythiofentanyl differs in substitution from fentanyl at the piperidine nitrogen atom. Fentanyl contains a phenyl ethyl group at the piperidine nitrogen atom whereas beta-hydroxythiofentanyl is substituted with a beta-hydroxy 2-thienyl ethyl group. Also, beta-hydroxythiofentanyl structurally differs from the schedule I synthetic opioid, thiofentanyl, by the addition of a hydroxyl group at the beta-position of the thienyl ethyl group. Data from postmortem toxicological analysis show that a fentanyl metabolite, norfentanyl, was detected in one case that involved beta-hydroxythiofentanyl. No study has been undertaken to evaluate the efficacy, toxicology, and safety of beta-hydroxythiofentanyl in humans. It can be inferred from medical examiner reports and data obtained from animal studies that beta-hydroxythiofentanyl has sufficient

distribution to the brain to produce depressant effects similar to that of mu opioid receptor agonists.

There is no FDA approved marketing application for a drug product containing beta-hydroxythiofentanyl for any therapeutic indication in the United States. Moreover, there are no clinical studies or petitioners of which has claimed an accepted medical use in the United States for this substance.

4. *Its History and Current Pattern of Abuse*: beta-Hydroxythiofentanyl was first encountered as a drug of abuse in 1985. Evidence suggests that the pattern of abuse of beta-hydroxythiofentanyl parallels that of prescription opioid analgesics. Beta-hydroxythiofentanyl, like other substances structurally related to fentanyl is disguised as a "legal" alternative to fentanyl. There is evidence that beta-hydroxythiofentanyl is ingested with other substances. beta-Hydroxythiofentanyl has been identified in pills, presumably intended for sale on the illicit market.

5. *The Scope, Duration, and Significance of Abuse*: beta-Hydroxythiofentanyl, similar to other substances structurally related to fentanyl, is a recreational drug. The recreational use of beta-hydroxythiofentanyl and other substances related to fentanyl continues to be of significant concern in the United States. These substances are distributed to users, often with unpredictable outcomes. Because users of beta-hydroxythiofentanyl and its associated drug products are likely to obtain these substances through unregulated sources, the identity, purity, and quantity are uncertain and inconsistent, thus posing significant adverse health risks to abusers. The significance of abuse for beta-hydroxythiofentanyl is reflected in the positive identification of this substance in several post-mortem cases. Though the scope and duration of abuse data for

beta-hydroxythiofentanyl were restricted to Florida in 2015, there is the possibility the number of fatalities were underreported because the capabilities of medical examiner offices across the country vary and many are unable to detect beta-hydroxythiofentanyl in their toxicological screens. Evidence that beta-hydroxythiofentanyl is being abused and trafficked is confirmed by law enforcement encounters. NFLIS contained ten reports of beta-hydroxythiofentanyl from Florida from State, local, and other forensic laboratories. These data demonstrate that beta-hydroxythiofentanyl has significance of abuse that supports its scheduling under the CSA.

Currently the United States is in the midst of a prescription and illicit opioid abuse epidemic. According to NFLIS, in the last few years, there has been marked increase in the encounters of synthetic opioids such as fentanyl and substances that are structurally related to fentanyl. In parallel to this increase in law enforcement encounters, there has been a corresponding marked increase in deaths related to synthetic opioids. beta-Hydroxythiofentanyl is a synthetic opioid that is structurally related to fentanyl. Therefore, the issue of fentanyl and substances structurally related to fentanyl abuse has become a major public health problem.

6. *What, if Any, Risk There is to the Public Health*: Available evidence on the overall public health risks associated with the use of beta-hydroxythiofentanyl is reflected by the several cases of fatalities (n=25) associated with its abuse. In addition to the recognized harm from ingesting beta-hydroxythiofentanyl, abusers risk harm when they obtain these drugs through unknown sources. Since beta-hydroxythiofentanyl shares a similar pharmacological profile with fentanyl and other opioid analgesics, individuals who abuse this substance are likely at risk of developing substance use disorder, overdose and death

similar to other opioid analgesics. Further, poly-substance abuse has been identified in fatalities involving fentanyl and other related opioids. In reported fatality cases involving beta-hydroxythiofentanyl, other substances such as cocaine, ethanol, other opioids, cannabinoids, benzodiazepines, and stimulants were also co-identified in the toxicological screening. Evidence suggests that products containing fentanyl related substances often do not bear accurate information regarding their contents and if they do, they may not contain the expected active ingredients or identify the health risks and potential hazards associated with these products. Thus, the limited knowledge about product contents, its purity and lack of information about its effects may pose another level of risk to users. Taken together, evidence posits that individuals experimenting with substances with unknown potency are at high risk of adverse health outcomes.

7. *Its Psychic or Physiological Dependence Liability*: There are no pre-clinical and clinical studies that have evaluated the dependence potential of beta-hydroxythiofentanyl. beta-Hydroxythiofentanyl is a mu-opioid receptor agonist, and discontinuation of the use of mu-opioid receptor agonists, such as fentanyl and morphine, is well known to cause withdrawal indicative of physical dependence. Opioid withdrawal includes nausea and vomiting, depression, agitation, anxiety, craving, sweats, hypertension, diarrhea, and fever.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled Under the CSA*: beta-Hydroxythiofentanyl is not considered an immediate precursor of any controlled substance of the CSA as defined by 21 U.S.C. 802(23).

Conclusion: After considering the scientific and medical evaluation conducted by the HHS, the HHS's recommendation, and the DEA's own eight-factor analysis, the DEA

finds that the facts and all relevant data constitute substantial evidence of the potential for abuse of beta-hydroxythiofentanyl. As such, the DEA hereby proposes to permanently schedule beta-hydroxythiofentanyl as a schedule I controlled substance under the CSA.

Proposed Determination of Appropriate Schedule

The CSA establishes five schedules of controlled substances known as schedules I, II, III, IV, and V. The CSA also outlines the findings required to place a drug or other substance in any particular schedule. 21 U.S.C. 812(b). After consideration of the analysis and recommendation of the Assistant Secretary for HHS and review of all other available data, the Acting Administrator of the DEA, pursuant to 21 U.S.C. 811(a) and 21 U.S.C. 812(b)(1), finds that:

1. beta-Hydroxythiofentanyl has a high potential for abuse;
2. beta- Hydroxythiofentanyl has no currently accepted medical use in treatment in the United States; and
3. There is a lack of accepted safety for use of beta-hydroxythiofentanyl under medical supervision.

Based on these findings, the Acting Administrator of the DEA concludes that beta-hydroxythiofentanyl (*N*-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-*N*-phenylpropionamide), including its isomers, esters, ethers, salts, and salts of isomers, esters and ethers, warrant continued control in schedule I of the CSA. 21 U.S.C. 812(b)(1).

Requirements for Handling beta-Hydroxythiofentanyl

If this rule is finalized as proposed, beta-hydroxythiofentanyl would continue[7] to be subject to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, dispensing, importing, exporting, research, and conduct of instructional activities, including the following:

1. *Registration.* Any person who handles (manufactures, distributes, dispenses, imports, exports, engages in research, or conducts instructional activities or chemical analysis with, or possesses) beta-hydroxythiofentanyl, or who desires to handle beta-hydroxythiofentanyl, is required to 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. *Security.* beta-Hydroxythiofentanyl is subject to schedule I security requirements and must be handled and stored pursuant to 21 U.S.C. 821, 823, and in accordance with 21 CFR 1301.71–1301.93.

3. *Labeling and Packaging.* All labels and labeling for commercial containers of beta-hydroxythiofentanyl must be in compliance with 21 U.S.C. 825 and 958(e), and be in accordance with 21 CFR part 1302.

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

5. *Inventory.* Any person registered with the DEA to handle beta-hydroxythiofentanyl must have an initial inventory of all stocks of controlled substances (including beta-hydroxythiofentanyl) on hand on the date the registrant first engages in

[7] beta-Hydroxythiofentanyl is currently subject to schedule I controls on a temporary basis, pursuant to 21 U.S.C. 811(h). 81 FR 29492, May. 12, 2016.

the handling of controlled substances pursuant to 21 U.S.C. 827 and 958, 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 beta-hydroxythiofentanyl) on hand every two years pursuant to 21 U.S.C. 827 and 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

6. *Records and Reports.* Every DEA registrant is required to maintain records and submit reports with respect to beta-hydroxythiofentanyl, pursuant to 21 U.S.C. 827 and 958(e), and in accordance with 21 CFR parts 1304 and 1312.

7. Order Forms. Every DEA registrant who distributes beta-hydroxythiofentanyl is required to comply with the order form requirements, pursuant to 21 U.S.C. 828, and 21 CFR part 1305.

8. Importation and Exportation. All importation and exportation of beta-hydroxythiofentanyl must be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

9. Liability. Any activity involving beta-hydroxythiofentanyl not authorized by, or in violation of, the CSA or its implementing regulations is unlawful, and could subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

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), this proposed scheduling action is subject to formal rulemaking procedures done "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 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 12866 and the principles reaffirmed in Executive Order 13563.

This proposed rule does not meet the definition of an Executive Order 13771 regulatory action, and the repeal and cost offset requirements of Executive Order 13771 have not been triggered. OMB has previously determined that formal rulemaking actions concerning the scheduling of controlled substances, such as this rule, are not significant regulatory actions under Section 3(f) of Executive Order 12866.

Executive Order 12988, Civil Justice Reform

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

Executive Order 13175, Consultation and Coordination with Indian Tribal Governments

This proposed rule does not have tribal implications warranting the application of Executive Order 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 Administrator, in accordance with the Regulatory Flexibility Act (RFA), 5 U.S.C. 601–602, has reviewed this proposed rule and by approving it, certifies that it will not have a significant economic impact on a substantial number of small entities. On May 12, 2016, the DEA published a final order to temporarily place beta-hydroxythiofentanyl in schedule I of the CSA pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). The DEA estimates that all entities handling or planning to handle beta-hydroxythiofentanyl have already established and implemented the systems and processes required to handle this substances. There are currently 15 registrations authorized to handle beta-hydroxythiofentanyl, as well as a number of registered analytical labs that are authorized to handle schedule I controlled substances generally. These 15 registrations represent 13 entities, of which 10 are small entities. Therefore, the DEA estimates 10 small entities are affected by this proposed rule.

A review of the 15 registrations indicates that all entities that currently handle beta-hydroxythiofentanyl also handle other schedule I controlled substances, and have established and implemented (or maintain) the systems and processes required to handle beta-hydroxythiofentanyl. Therefore, the DEA anticipates that this proposed rule will

impose minimal or no economic impact on any affected entities; and thus, will not have a significant economic impact on any of the 10 affected small entities. Therefore, the DEA has concluded that this proposed rule will not have a significant effect on a substantial number of small entities.

Unfunded Mandates Reform Act of 1995

In accordance with the Unfunded Mandates Reform Act (UMRA) of 1995, 2 U.S.C. 1501 *et seq.*, the DEA has determined and certifies 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 $100,000,000 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 under the Paperwork Reduction Act of 1995. 44 U.S.C. 3501–3521. This action would 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.

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 proposes to amend 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)(15) through (60) as (b)(16) through (61); and

b. Add new paragraph (b)(15);

c. Remove and reserve paragraph (h)(3).

The addition to read as follows:

§ 1308.11 Schedule I.

* * * * *

(b) * * *

(15) *N*-[1-[2-hydroxy-2-(thiophen-2-yl)ethyl]piperidin-4-yl]-*N*-phenylpropionamide, its isomers, esters, ethers, salts and salts of isomers, esters and ethers (Other name: beta-Hydroxythiofentanyl)…….....(9836)

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Dated: May 7, 2018

Robert W. Patterson,
Acting Administrator.
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