DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA–900N]

Schedules of Controlled Substances: Placement of Butonitazene, Flunitazene, and Metodesnitazene Substances in Schedule I

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration proposes placing butonitazene, flunitazene, and metodesnitazene including their isomers, esters, ethers, salts and salts of isomers, esters and ethers in schedule I of the Controlled Substances Act. If finalized, this action would make permanent the existing regulatory controls and administrative, civil, and criminal sanctions applicable to schedule I controlled substances on persons who handle (manufacture, distribute, reverse distribute, import, export, engage in research, conduct instructional activities or chemical analysis with, or possess), or propose to handle these three specific controlled substances.

DATES: Comments must be submitted electronically or postmarked on or before May 13, 2024.

Interested persons may file a request for a hearing or waiver of hearing pursuant to 21 CFR 1308.44 and in accordance with 21 CFR 1316.47 and/or 1316.49, as applicable. Requests for a hearing, and waivers of an opportunity for a hearing or to participate in a hearing, must be received on or before May 13, 2024.

ADDRESSES: Interested persons may file written comments on this proposal in accordance with 21 CFR 1308.43(g). 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–900N'' on all electronic and written correspondence, including any attachments.

• *Electronic comments:* The Drug Enforcement Administration (DEA) encourages commenters to submit all comments 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 *https://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. If you have received a Comment Tracking Number, your comment has been successfully submitted and there is no need to resubmit the same comment. 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.

• *Paper comments:* Paper comments that duplicate electronic submissions 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 Morrissette Drive, Springfield, Virginia 22152.

• *Hearing requests:* All requests for a hearing and waivers of participation, together with a written statement of position on the matters of fact and law asserted in the hearing, must be filed with the DEA Administrator, who will make the determination of whether a hearing will be needed to address such matters of fact and law in the rulemaking. Such requests must be sent to: Drug Enforcement Administration, Attn: Administrator, 8701 Morrissette Drive, Springfield, Virginia 22152. For informational purposes, a courtesy copy of requests for hearing and waivers of participation should also be sent to: (1) Drug Enforcement Administration, Attn: Hearing Clerk/OALJ, 8701 Morrissette Drive, Springfield, Virginia 22152; and (2) Drug Enforcement Administration, Attn: DEA Federal Register Representative/DPW, 8701 Morrissette Drive, Springfield, Virginia 22152.

• *Paperwork Reduction Act Comments:* All comments concerning collections of information under the Paperwork Reduction Act must be submitted to the Office of Information and Regulatory Affairs, OMB, Attention: Desk Officer for DOJ, Washington, DC 20503. Please state that your comment refers to Docket No. DEA–900N.

FOR FURTHER INFORMATION CONTACT: Dr. Terrence L. Boos, Drug and Chemical Evaluation Section, Diversion Control Division, Drug Enforcement Administration; Telephone: (571) 362–3249.

SUPPLEMENTARY INFORMATION: In this proposed rule, the Drug Enforcement Administration (DEA) proposes to permanently schedule the following three controlled substances in schedule I of the Controlled Substances Act (CSA), including their isomers, esters, ethers, salts, and salts of isomers, esters, and ethers whenever the existence of such isomers, esters, ethers, and salts is possible within the specific chemical designation:

• butonitazene (2-(2-(4-butoxybenzyl)-5-nitro-1*H*-benzimidazol-1-yl)-*N,N*-diethylethan-1-amine),

• flunitazene (*N,N*-diethyl-2-(2-(4-fluorobenzyl)-5-nitro-1*H*-benzimidazol-1-yl)ethan-1-amine),

• metodesnitazene (*N,N*-diethyl-2-(2-(4-methoxybenzyl)-1*H*-benzimidazol-1-yl)ethan-1-amine).

Posting of Public Comments

All comments received in response to this docket are considered part of the public record. DEA will make comments available for public inspection online at *https://www.regulations.gov,* unless reasonable cause is given. Such information includes personal or business identifiers (such as name, address, state of federal identifiers, etc.) voluntarily submitted by the commenter.

Commenters submitting comments which include personal identifying information (PII), confidential, or proprietary business information that the commenter does not want made publicly available should submit two copies of the comment. One copy must be marked ''CONTAINS CONFIDENTIAL INFORMATION'' and should clearly identify all PII or business information the commenter does not want to be made publicly available, including any supplemental materials. DEA will review this copy, including the claimed PII and confidential business information, in its consideration of comments. The second copy should be marked ''TO BE PUBLICLY POSTED'' and must have all claimed confidential PII and business information already redacted. DEA will post only the redacted comment on *https://www.regulations.gov* for public inspection. DEA generally will not redact additional information contained in the comment marked ''TO BE PUBLICLY POSTED.'' The Freedom of Information Act applies to all comments received.

For easy reference, an electronic copy of this document and supplemental information to this proposed scheduling action are available at *https://www.regulations.gov.*

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.[1] Interested persons, as defined in 21 CFR 1300.01(b), may file requests for a hearing in conformity with the requirements of 21 CFR 1308.44(a) and 1316.47(a), and such requests must:

(1) state with particularity the interest of the person in the proceeding;

(2) state with particularity the objections or issues concerning which the person desires to be heard; and

(3) state briefly the position of the person with regarding to the objections or issues.

Any interested person may file a waiver of an opportunity for a hearing or to participate in a hearing in conformity with the requirements of 21 CFR 1308.44(c), together with a written statement of position on the matters of fact and law involved in any hearing.[2]

All requests for a hearing and waivers of participation, together with a written statement of position on the matters of fact and law involved in such hearing, must be sent to DEA using the address information provided above. The decision whether a hearing will be needed to address such matters of fact and law in the rulemaking will be made by the Administrator. If a hearing is needed, DEA will publish a notice of hearing on the proposed rulemaking in the **Federal Register**.[3] Further, once the Administrator determines a hearing is needed to address such matters of fact and law in rulemaking, she will then designate an Administrative Law Judge (ALJ) to preside over the hearing. The ALJ's functions shall commence upon designation, as provided in 21 CFR 1316.52.

In accordance with 21 U.S.C. 811 and 812, the purpose of a hearing would be to determine whether butonitazene, flunitazene, and metodesnitazene meet the statutory criteria for placement in schedule I, as proposed in this rule.

Legal Authority

The 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 (delegated to the Administrator of DEA pursuant to 28 CFR 0.100) on his own motion, at the request of the Secretary of Health and Human Services (HHS), or on the petition of any interested party.[4] This proposed action is supported by a recommendation from the Assistant Secretary for Health of HHS (Assistant Secretary for HHS or Assistant Secretary) and an evaluation of all other relevant data by DEA. If finalized, this action would make permanent the existing temporary regulatory controls and administrative, civil, and criminal sanctions of schedule I controlled substances on any person who handles or proposes to handle these three substances.

Background

On April 12, 2022, pursuant to 21 U.S.C. 811(h)(1), DEA published an order in the **Federal Register** temporarily placing butonitazene, flunitazene, metodesnitazene, and four additional benzimidazole-opioids in schedule I of the Controlled Substances Act (CSA) based upon a finding that these substances pose an imminent hazard to the public safety.[5] That temporary order was effective upon the date of publication. Under 21 U.S.C. 811(h)(2), the temporary scheduling of a substance expires at the end of two years from the date of issuance of the scheduling order, except that DEA may extend temporary scheduling of that substance for up to one year during the pendency of permanent scheduling proceedings under 21 U.S.C. 811(a)(1) with respect to the substance. Pursuant to 21 U.S.C. 811(h)(2), the temporary scheduling of butonitazene, flunitazene, and metodesnitazene expires on April 12, 2024, unless extended. An extension of the temporary order is being ordered by the DEA Administrator in a separate action, published elsewhere in this issue of the **Federal Register**.

As described in the temporary order published on April 12, 2022, butonitazene, flunitazene, and metodesnitazene belong to the class of substances known as benzimidazole-opioids and are synthetic opioids. The Assistant Secretary for HHS has advised DEA that there are no exemptions or approvals in effect for butonitazene, flunitazene, and metodesnitazene under section 505 of the Federal Food, Drug and Cosmetic Act, 21 U.S.C. 335. According to HHS, and also by DEA's findings in this proposed rule, butonitazene, flunitazene, and metodesnitazene have no known accepted medical use. These substances are not the subject of any approved new drug application (NDA) or investigational new drug application (IND), and are not currently marketed as approved drug products.

The Administrator, on her own motion pursuant to 21 U.S.C. 811(a), is initiating proceedings to permanently schedule butonitazene, flunitazene, and metodesnitazene. DEA gathered the necessary data and reviewed the available information regarding the pharmacology, chemistry, trafficking, actual abuse, pattern of abuse, and the relative potential for abuse for these substances. On July 13, 2022, in accordance with 21 U.S.C. 811(b), the Administrator then submitted a request to the Assistant Secretary to provide DEA with a scientific and medical evaluation of available information and a scheduling recommendation for six benzimidazole substances.

On November 15, 2023, the Assistant Secretary submitted HHS's scientific and medical evaluation and scheduling recommendation for butonitazene, flunitazene, metodesnitazene, and three other benzimidazole-opioids and their salts to the Administrator,[6] which recommended placing butonitazene, flunitazene, and metodesnitazene and their salts in schedule I of the CSA. In accordance with 21 U.S.C. 811(c), upon receipt of the scientific and medical evaluation and scheduling recommendation from HHS, DEA reviewed the documents and all other relevant data, and conducted its own eight-factor analysis of the abuse potential of these three substances.

Proposed Determination to Permanently Schedule Butonitazene, Flunitazene, and Metodesnitazene

As discussed in the background section, the Administrator is initiating proceedings, pursuant to 21 U.S.C. 811(a), to permanently add butonitazene, flunitazene, and metodesnitazene to schedule I. DEA reviewed the scientific and medical evaluation and scheduling recommendation received from HHS, and all other relevant data, and it conducted its own eight-factor analysis of the abuse potential of these three

[1] 21 CFR 1308.41 through 1308.45; 21 CFR part 1316, subpart D.

[2] 21 CFR 1316.49.

[3] 21 CFR 1308.44(b), 1316.53.

[4] 21 U.S.C. 811(a).

[5] *See* Schedules of Controlled Substances: Temporary Placement of Butonitazene, Etodesnitazene, Flunitazene, Metodesnitazene, Metonitazene, *N*-Pyrrolidino etonitazene, and Protonitazene in Schedule I, 87 FR 21556 (Apr. 12, 2022). The four additional benzimidazole-opioids were etodesnitazene, metonitazene, *N*-pyrrolidino etonitazene, and protonitazene. DEA pursued separate scheduling actions for metonitazene, *see* 88 FR 56466 (Aug. 18, 2023) and for etodesnitazene, *N*-pyrrolidino etonitazene, and protonitazene, to remain as a schedule I substances under the CSA in order to meet the United States' obligations under the United Nations Single Convention on Narcotic Drugs, Mar. 30, 1961, 18 U.S.T. 1407, 520 U.N.T.S. 151 (Single Convention), as amended by the 1972 Protocol.

[6] The three other benzimidazole-opioids (etodesnitazene, *N*-pyrrolidino etonitazene, and protonitazene) will not be discussed further in this proposed rule.

substances pursuant to 21 U.S.C. 811(c). Included below is a brief summary of each factor as analyzed by HHS and DEA, and as considered by DEA in its proposed scheduling action. Please note that both the DEA and HHS analyses are available in their entirety under ''Supporting Documents'' of the public docket for this proposed rule at *https://www.regulations.gov* under Docket Number ''DEA–900N.''

1. The Drug's Actual or Relative Potential for Abuse

In addition to considering the information HHS provided in its scientific and medical evaluation document for butonitazene, flunitazene, and metodesnitazene, DEA also considered all other relevant data regarding actual or relative potential for abuse of these three substances. The term ''abuse'' is not defined in the CSA; however, the legislative history of the CSA suggests that DEA consider the following criteria when determining whether a particular drug or substance has a potential for abuse: [7]

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

b. There is a significant diversion of the drug or 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.

Both DEA and HHS eight-factor analyses found that butonitazene, flunitazene, and metodesnitazene have pharmacological profiles similar to those of the synthetic opioids etonitazene and isotonitazene, which are both schedule I controlled substances and have high potential for abuse. According to HHS, butonitazene, flunitazene, and metodesnitazene have no approved medical uses in the United States, and they have been encountered on the illicit drug market with adverse outcomes on the public health and safety. Because there are no Food and Drug Administration (FDA)-approved or FDA-exempted products for butonitazene, flunitazene, and metodesnitazene in the United States or in any other country, a practitioner may not legally prescribe them, and they cannot be dispensed to an individual. However, these benzimidazole-opioids substances are available for purchase from legitimate chemical companies because they can be used in scientific research. There is no known diversion from research activities for these substances.

Because butonitazene, flunitazene, and metodesnitazene are not formulated or available for clinical use as approved medicinal products, it is inferred that all current use of these substances by individuals are based on their own initiative, rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs. According to drug seizure data from 2020 and 2023 from the National Forensic Laboratory Information System (NFLIS-Drug) [8] database, which collects drug identification results from drug cases submitted to and analyzed by Federal, State, and local forensic laboratories, there have been a total of 130 reports for butonitazene, flunitazene, or metodesnitazene. Evidence from law enforcement seizures [9] indicate that individuals are taking these benzimidazole-opioids with no accepted medical use, on their own initiative rather than on the medical advice of a licensed practitioner. Individuals may be using these benzimidazole-opioids on their own initiative because of their opioidergic effects similar to other schedule I or II opioid substances. Consequently, law enforcement encounters of butonitazene, flunitazene, and metodesnitazene demonstrate that these substances are being abused, and thus pose safety hazards to the health of users or the community.

2. Scientific Evidence of the Drug's Pharmacological Effects, if Known

According to DEA and HHS, the pharmacological activity of butonitazene, flunitazene, and metodesnitazene in humans is unknown. Preclinical studies show that these benzimidazole-opioids exhibit a pharmacological profile similar to that of morphine and fentanyl. As explained in detail in both DEA and HHS eight-factor analyses, data from binding studies show that these substances, similar to morphine and fentanyl, selectively bound to mu-opioid receptors.[10] In opioid receptor functional assays, butonitazene, flunitazene, and metodesnitazene, similar to fentanyl and morphine, acted as mu-opioid receptor agonists.[11] Further, data from preclinical studies using rodents showed that butonitazene, flunitazene, and metodesnitazene, similar to morphine and fentanyl, produced analgesic effects that can be attenuated by an opioid antagonist pretreatment.[12] [13] HHS concluded that, similar to morphine and fentanyl, butonitazene, flunitazene, and metodesnitazene produced analgesic effects via activation of mu-opioid receptors.

Additionally, behavioral effects of butonitazene, flunitazene, and metodesnitazene were assessed using the drug discrimination model. Drug discrimination studies can be used to determine whether a test drug produces pharmacological effects (*i.e.,* interoceptive stimulus effects) similar to those produced by a known drug of abuse. Drugs that produce stimulus effects similar to known drugs of abuse in animals are also likely to be abused by humans. As explained in detail in both DEA and HHS eight-factor analyses, data from drug discrimination

[7] 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.

[8] NFLIS-Drug represents an important resource in monitoring illicit drug trafficking, including the diversion of legally manufactured pharmaceuticals into illegal markets. NFLIS-Drug is a comprehensive information system that includes data from forensic laboratories that handle the nation's drug analysis cases. NFLIS-Drug participation rate, defined as the percentage of the national drug caseload represented by laboratories that have joined NFLIS, is currently 98.5 percent. NFLIS includes drug chemistry results from completed analyses only. NFLIS-Drug data was queried on November 21, 2023.

[9] 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* Schedules of Controlled Substances: Placement of Carisoprodol Into Schedule IV, 76 FR 77330, 77332 (Dec. 12, 2011).

[10] DEA–VA Interagency Agreement. ''In Vitro Receptor and Transporter Assays for Abuse Liability Testing for the DEA by the VA''. Binding and Functional Activity at Delta, Kappa and Mu Opioid Receptors. 2020. Unpublished data.

[11] DEA–VA Interagency Agreement. ''In Vitro Receptor and Transporter Assays for Abuse Liability Testing for the DEA by the VA''. Binding and Functional Activity at Delta, Kappa and Mu Opioid Receptors. 2021. Unpublished data.

[12] Gatch MB. Evaluation of Abuse Potential of Synthetic Opioids Using in Vivo Pharmacological Studies. Test of analgesic effects alone and in combination with naltrexone. Unpublished Data. 2022.

[13] Paronis C. Evaluation of Synthetic Opioid Substances using Analgesia and Drug Discrimination Assays. Test of antinociceptive effects. Unpublished Data. 2021a.

studies demonstrate that butonitazene,[14] flunitazene,[15] and metodesnitazene [16] have stimulus properties that are similar to both morphine and fentanyl, schedule II drugs. Taken together, data from preclinical studies demonstrate that butonitazene, flunitazene, and metodesnitazene share similarities in their pharmacological effects and mechanism of action to the schedule II opioid drugs morphine and fentanyl.

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

Butonitazene, flunitazene, and metodesnitazene belong to the 2-benzylbenzimidazole structural class. The chemical structures of these 2-benzylbenzimidazoles contain a benzimidazole ring and a benzyl group at the benzimidazole 2-position. These benzimidazole-opioids are structurally related to several schedule I substances, including etonitazene. There are no FDA-approved marketing applications for drug products containing butonitazene, flunitazene, and metodesnitazene for any therapeutic indication in the United States or medical use in any other country. Further, there are no well-controlled clinical studies that have demonstrated the safety or efficacy for these substances. According to HHS, FDA concluded that butonitazene, flunitazene, and metodesnitazene have no currently accepted medical use in the United States. Similarly, DEA concludes that butonitazene, flunitazene, and metodesnitazene have no currently accepted medical use according to established DEA procedure and case law.

4. Its History and Current Pattern of Abuse

In the late 1950s, the Swiss chemical company CIBA Aktiengesellschaft synthesized a group of benzimidazole derivatives with analgesic properties; [17] however, the research did not lead to any medically approved analgesic products. These benzimidazole derivatives include schedule I substances, such as the synthetic opioids clonitazene, etonitazene, and isotonitazene. In 2019, isotonitazene emerged on the illicit drug market and was involved in numerous fatal overdose events; in August 2020, it was temporarily controlled as a schedule I substance under the CSA.[18] Subsequently, additional six benzimidazole-opioids emerged on the illicit opioid drug market. In April 2022, DEA temporarily controlled these six benzimidazole-opioids as schedule I substances due, in part, to their involvement in numerous postmortem and toxicology cases.[19] Law enforcement agencies have encountered butonitazene, flunitazene, and metodesnitazene in several solid (*e.g.,* powder, rock, and tablet) forms. These substances are not approved for medical use anywhere in the world.

According to HHS, there are no FDA-approved drug products for butonitazene, flunitazene, and metodesnitazene in the United States.[20] The appearance of these benzimidazole-opioids on the illicit drug market is similar to other synthetic opioids that are trafficked for their psychoactive effects. These three benzimidazole-opioid substances are likely to be abused in the same manner as schedule I opioids, such as etonitazene, isotonitazene, and heroin. These substances have been identified as powders or tablets, typically of unknown purity or concentration. Between 2020 and 2021, butonitazene, flunitazene, and metodesnitazene emerged on the illicit synthetic drug market as evidenced by their identification in forensic drug seizures and in biological samples. Based on NFLIS-Drug data, law enforcement encounters of butonitazene, flunitazene, and metodesnitazene often included mixtures. Substances found in combination with some of these benzimidazole-opioids include other substances of abuse, such as heroin, fentanyl, fentanyl analogues, designer benzodiazepines, and cocaine.

5. The Scope, Duration, and Significance of Abuse

Butonitazene, flunitazene, and metodesnitazene, similar to schedule I substances, such as etonitazene and isotonitazene, are synthetic opioids, and evidence suggests they are abused for their opioidergic effects. The abuse of these benzimidazole-opioids, similar to other synthetic opioids, has resulted in their identification in toxicology, post-mortem cases, and law enforcement encounters. Data from the toxicology analysis showed that butonitazene has been positively identified in three postmortem cases, flunitazene in four post mortem cases,[21] and metodesnitazene in one case.[22]

Data from law enforcement suggest that butonitazene, flunitazene, and metodesnitazene are being abused in the United States as recreational drugs. The law enforcement encounters of these benzimidazole-opioids, as reported to NFLIS-Drug, included 130 exhibits since 2020. NFLIS-Drug registered 66 encounters of butonitazene from 7 states, 60 encounters of flunitazene from 11 states, and 4 encounters of metodesnitazene from 3 states. Of the 66 reports involving butonitazene, fentanyl was co-identified in 24 cases. Flunitazene was commonly co-identified with metonitazene (n = 30) in fifty percent of the cases. Metodesnitazene was co-reported with diphenhydramine (n = 2), fentanyl (n = 2), and heroin (n = 2).

The identification of these benzimidazole-opioids in forensic and toxicology cases suggests they may be presented as a substitute for heroin or fentanyl and likely abused in the same manner as either of those substances. The population likely to be harmed by these benzimidazole-opioids appears to be the same as that harmed by other opioid substances, such as heroin, tramadol, fentanyl, and other synthetic opioid substances. This is evidenced by the types of other drugs co-identified in biological samples and law enforcement encounters. Law enforcement and toxicology reports demonstrate that butonitazene, flunitazene, and metodesnitazene are being abused, and that their use can produce serious adverse events that can lead to death. Because users of butonitazene, flunitazene, and metodesnitazene are likely to obtain these substances through unregulated sources, the identity, purity, and quantity of these substances are uncertain and likely to be inconsistent, thus posing significant adverse health risks to the end user. Individuals who initiate use of one or more of these benzimidazole-opioids are likely to be at risk of developing a substance use disorder, fatal or non-fatal

[14] Gatch, M. Butonitazene: Test of substitution for the discriminative stimulus effects of morphine (15DDHQ21F00000340, 2021. Unpublished Data).

[15] Paronis, C. Flunitazene: Test of morphine-like discriminative stimulus effects (15DDHQ20P00000709, 2021b. Unpublished Data).

[16] Paronis, C. Metodesnitazene: Test of morphine-like discriminative stimulus effects (15DDHQ20P00000709, 2021c. Unpublished Data).

[17] Hunger, A., Kebrle, J., Rossi, A., & Hoffmann, K. [Synthesis of analgesically active benzimidazole derivatives with basic substitutions]. Experientia, 1957 Oct 15;13(10), 400–401.

[18] 85 FR 51342 (Aug. 20, 2020).

[19] 87 FR 21556 (Apr. 12, 2022).

[20] Department of Health and Human Services. Basis for the Recommendation to Control Butonitazene, Etodesnitazene, Flunitazene, Metodesnitazene, N-Pyrrolidino Etonitazene, and Protonitazene and Their Salts in Schedule I of the Controlled Substances Act (November 2023).

[21] Walton SE, Krotulski AJ, Logan BK. A Forward-Thinking Approach to Addressing the New Synthetic Opioid 2-Benzylbenzimidazole Nitazene Analogs by Liquid Chromatography—Tandem Quadrupole Mass Spectrometry (LC–QQQ–MS). J Anal Toxicol. 2022 Mar 21;46(3):221–231.

[22] Metodesnitazene_092221_ToxicologyAnalyticalReport.pdf (*cfsre.org*).

overdose, similar to that of other opioid analgesics (*e.g.,* fentanyl, morphine, etc.).

6. What, if Any, Risk There Is to the Public Health

The increase in opioid overdose deaths in the United States has been exacerbated recently by the availability of potent synthetic opioids on the illicit drug market. It is well established that substances that act as mu-opioid receptor agonists have a high potential for abuse and addiction and can induce dose-dependent respiratory depression. As with any mu-opioid receptor agonist, the potential health and safety risks for users of butonitazene, flunitazene, and metodesnitazene are high. Consistently, these three benzimidazole-opioids have been positively identified in toxicology cases. The public health risks associated with the abuse of mu-opioid receptor agonists are well established.

The introduction of synthetic opioids, such as butonitazene, flunitazene, and metodesnitazene, into the illicit drug market may serve as a portal to problematic opioid use for those seeking these opioids. Evidence from toxicology reports show that poly-substance abuse remains common in fatalities associated with the abuse of some of these benzimidazole-opioids.

7. Its Psychic or Physiological Dependence Liability

Butonitazene, flunitazene, and metodesnitazene have pharmacological effects similar to those of schedule I benzimidazole-opioids such as clonitazene, etonitazene, and isotonitazene. According to HHS, analgesic studies conducted on these benzimidazole-opioids show that they produce effects similar to that of either morphine or fentanyl, both schedule II narcotic drugs. Although there are no clinical studies that have evaluated the dependence potential of these substances, they are mu-opioid receptor agonists, and it is well known that the discontinuation of the use of mu-opioid receptor agonists, such as fentanyl and morphine, causes withdrawal symptoms indicative of physical dependence. The similarities in the pharmacological profile and pattern of abuse of these benzimidazole-opioids, heroin, and fentanyl are indicative of their similar potential to have psychic and physiological dependence liability.

8. Whether the Substance Is an Immediate Precursor of a Substance Already Controlled Under the CSA

Butonitazene, flunitazene, and metodesnitazene are not immediate precursors of a substance controlled under the CSA, as defined by 21 U.S.C. 802(23).

Conclusion:

After considering the scientific and medical evaluation and accompanying scheduling recommendation of HHS, and DEA's own eight-factor analysis, DEA finds that these facts and all relevant data constitute substantial evidence of potential for abuse of butonitazene, flunitazene, and metodesnitazene. As such, DEA proposes to permanently schedule these three benzimidazole-opioids as schedule I controlled substances 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.[23] After consideration of the analysis and recommendation of the Assistant Secretary for HHS and review of all other available data, the Administrator of DEA, pursuant to 21 U.S.C. 811(a) and 812(b)(1), finds that:

(1) Butonitazene, flunitazene, and metodesnitazene have a high potential for abuse. Butonitazene, flunitazene, and metodesnitazene, similar to etonitazene and fentanyl, are mu-opioid receptor agonists. These three benzimidazole-opioids have analgesic effects and these effects are mediated by mu-opioid receptor agonism. HHS states that substances that produce mu-opioid receptor agonist effects in the central nervous system are considered as having a high potential for abuse (*e.g.* morphine and fentanyl). Data obtained from drug discrimination studies indicate that butonitazene, flunitazene, and metodesnitazene fully substituted for the discriminative stimulus effects of morphine.

(2) Butonitazene, flunitazene, and metodesnitazene have no currently accepted medical use in the United States. There are no FDA-approved drug products for butonitazene, flunitazene, and metodesnitazene in the United States. There are no known therapeutic applications for these benzimidazole-opioids and DEA is not aware of any currently accepted medical uses for these substances in the United States.[24]

(3) There is a lack of accepted safety for use of butonitazene, flunitazene, and metodesnitazene under medical supervision. Because these substances have no FDA-approved medical use and have not been investigated as new drugs, their safety for use under medical supervision is not determined.

Based on these findings, the Administrator of DEA concludes that butonitazene, flunitazene, and metodesnitazene, including their isomers, esters, ethers, salts, and salts of isomers, esters, and ethers whenever the existence of such isomers, esters, ethers, and salts is possible within the specific chemical designation, warrant continued control in schedule I of the CSA.[25]

Requirements for Handling Butonitazene, Flunitazene, and Metodesnitazene

As discussed above, these three substances are currently subject to a temporary scheduling order, which added them to schedule I. If this rule is finalized as proposed, butonitazene, flunitazene, and metodesnitazene would be subject, on a permanent basis, to the CSA's schedule I regulatory controls and administrative, civil, and criminal sanctions applicable to the manufacture, distribution, reverse distribution, dispensing, importation, exportation, engagement in research, and conduct of instructional activities or chemical analysis with, and possession of schedule I 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) butonitazene, flunitazene, and metodesnitazene 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. *Security.* Butonitazene, flunitazene, and metodesnitazene are subject to schedule I security requirements and must be handled and stored pursuant to 21 U.S.C. 821, 823, and 871(b), and in accordance with 21 CFR 1301.71 through 1301.76. Non-practitioners

[23] 21 U.S.C. 812(b).

[24] HHS and DEA both applied a five-part test for currently accepted medical use as part of this scheduling action. Under that test, with respect to a drug that has not been approved by the Food and Drug Administration, to have a currently accepted medical use in treatment in the United States, all of the following must be demonstrated: i. The drug's chemistry must be known and reproducible; ii. there must be adequate safety studies; iii. there must be adequate and well-controlled studies proving efficacy; iv. the drug must be accepted by qualified experts; and v. the scientific evidence must be widely available. Marijuana Scheduling Petition; Denial of Petition; Remand, 57 FR 10499 (Mar. 26, 1992), *pet. for rev. denied, Alliance for Cannabis Therapeutics* v. *Drug Enforcement Admin.,* 15 F.3d 1131, 1135 (D.C. Cir. 1994).

[25] 21 U.S.C. 812(b)(1).

handling these three substances also must comply with the screening requirements of 21 CFR 1301.90 through 1301.93.

3. Labeling and Packaging. All labels and labeling for commercial containers of butonitazene, flunitazene, and metodesnitazene must comply 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 butonitazene, flunitazene, and metodesnitazene 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 DEA to handle butonitazene, flunitazene, and metodesnitazene must have an initial inventory of all stocks of controlled substances (including these substances) on hand on the date the registrant first engages in 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 butonitazene, flunitazene, and metodesnitazene) 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 must maintain records and submit reports with respect to butonitazene, flunitazene, and metodesnitazene, pursuant to 21 U.S.C. 827, 832(a), and 958(e), and in accordance with 21 CFR 1301.74(b) and (c) and 1301.76(b) and 21 CFR parts 1304, 1312, and 1317. Manufacturers and distributors would be required to submit reports regarding butonitazene, flunitazene, and metodesnitazene to the Automation of Reports and Consolidated Order System pursuant to 21 U.S.C. 827, and in accordance with 21 CFR parts 1304 and 1312.

7. Order Forms. Every DEA registrant who distributes butonitazene, flunitazene, and metodesnitazene must 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 butonitazene, flunitazene, and metodesnitazene must comply with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

9. Liability. Any activity involving butonitazene, flunitazene, and metodesnitazene 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

Executive Orders 12866 (Regulatory Planning and Review), 13563 (Improving Regulation and Regulatory Review), and 14094 (Modernizing Regulatory Review)

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 (E.O.) 12866 and the principles reaffirmed in E.O. 13563. E.O. 14094 modernizes the regulatory review process to advance policies that promote the public interest and address national priorities.

Executive Order 12988, Civil Justice Reform

This proposed 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.

Executive Order 13132, Federalism

This proposed rulemaking does not have federalism implications warranting the application of E.O. 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 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 Administrator, in accordance with the Regulatory Flexibility Act, 5 U.S.C. 601–612, has reviewed this rule and, by approving it, certifies that it will not have a significant economic impact on a substantial number of small entities.

On April 12, 2022, DEA published an order to temporarily place seven benzimidazole-opioids in schedule I of the CSA pursuant to the temporary scheduling provisions of 21 U.S.C. 811(h). DEA estimates that all entities handling or planning to handle butonitazene, flunitazene, and metodesnitazene have already established and implemented systems and processes required to handle these substances.

There are currently 45 registrations authorized to specifically handle butonitazene, flunitazene, or metodesnitazene, as well as 1,239 registered analytical labs and 861 researchers that are authorized to handle schedule I controlled substances generally. These 45 registrations represent 31 entities. A review of the 45 registrations indicates that all entities that currently handle butonitazene, flunitazene, and metodesnitazene also handle other schedule I controlled substances and have established and implemented (or maintained) systems and processes required to handle these substances. Therefore, DEA anticipates 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 affected small entity. Therefore, DEA has concluded that this proposed rule will not have a significant economic impact 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.,* 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 annually for inflation) in any 1 year. . . .'' Therefore, neither a Small Government Agency Plan nor any other action is required under UMRA of 1995.

Paperwork Reduction Act of 1995

This proposed rule would not impose a new collection or modify an existing collection of information under the Paperwork Reduction Act of 1995.[26] Also, this proposed rule would not impose new or modify existing recordkeeping or reporting requirements on state or local governments,

[26] 44 U.S.C. 3501–3521.

individuals, businesses, or organizations. However, this proposed rule would require compliance with the following existing OMB collections: 1117–0003, 1117–0004, 1117–0006, 1117–0008, 1117–0009, 1117–0010, 1117–0012, 1117–0014, 1117–0021, 1117–0023, 1117–0029, and 1117–0056. 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.

Signing Authority

This document of the Drug Enforcement Administration was signed on April 5, 2024, by Administrator Anne Milgram. That document with the original signature and date is maintained by DEA. For administrative purposes only, and in compliance with requirements of the Office of the Federal Register, the undersigned DEA Federal Register Liaison Officer has been authorized to sign and submit the document in electronic format for publication, as an official document of DEA. This administrative process in no way alters the legal effect of this document upon publication in the **Federal Register**.

Scott Brinks,

Federal Register Liaison Officer, Drug Enforcement Administration.

For the reasons set out above, DEA proposes to amend 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. In § 1308.11:

■ a. Redesignate paragraphs (b)(62) through (107) as paragraphs (b)(66) through (110);

■ b. Redesignate paragraphs (b)(44) through (62) as paragraphs (b)(46) through (64);

■ c. Redesignate paragraphs (b)(24) through (43) as paragraphs (b)(25) through (44);

■ d. Add new paragraphs (b)(24), (45), and (65); and

■ e. Remove and reserve paragraphs (h)(50), (52), and (53).

The additions to read as follows:

§ 1308.11 Schedule I.

* * * * *

(b) * * *

* * * * * * *	
(24) Butonitazene (2-(2-(4-butoxybenzyl)-5-nitro-1*H*-benzimidazol-1-yl)-*N,N*-diethylethan-1-amine)	9751
* * * * * * *	
(45) Flunitazene (*N,N*-diethyl-2-(2-(4-fluorobenzyl)-5-nitro-1*H*-benzimidazol-1-yl)ethan-1-amine)	9756
* * * * * * *	
(65) Metodesnitazene (*N,N*-diethyl-2-(2-(4-methoxybenzyl)-1*H*-benzimidazol-1-yl)ethan-1-amine)	9764

* * * * *

[FR Doc. 2024–07694 Filed 4–10–24; 8:45 am]

BILLING CODE 4410–09–P

DEPARTMENT OF THE TREASURY

Internal Revenue Service

26 CFR Part 1

[REG–100908–23]

RIN 1545–BQ62

Increased Credit or Deduction Amounts for Satisfying Certain Prevailing Wage and Registered Apprenticeship Requirements; Correction

AGENCY: Internal Revenue Service (IRS), Treasury.

ACTION: Notice of proposed rulemaking; correction.

SUMMARY: This document corrects a notice of proposed rulemaking (REG–100908–23) published in the **Federal Register** on August 30, 2023, containing proposed regulations regarding increased credit or deduction amounts available for taxpayers satisfying prevailing wage and registered apprenticeship (collectively, PWA) requirements established by the Inflation Reduction Act of 2022 (IRA).

DATES: Written or electronic comments were to be received by October 30, 2023.

ADDRESSES: Commenters were strongly encouraged to submit public comments electronically.

FOR FURTHER INFORMATION CONTACT: Concerning the proposed regulations, the Office of Associate Chief Counsel (Passthroughs & Special Industries) at (202) 317–6853 (not a toll-free number); concerning submissions of comments or the public hearing, Vivian Hayes, (202) 317–6901 (not toll-free number) or by email to *publichearings@irs.gov* (preferred).

SUPPLEMENTARY INFORMATION:

Background

The notice of proposed rulemaking (REG–100908–23) that is the subject of this correction is under sections 30C, 45, 45L, 45Q, 45U, 45V, 45Y, 45Z, 48C, 48E, and 179D of the Code.

Need for Correction

As published, the notice of proposed rulemaking (REG–100980–23) contains an error that needs to be corrected.

Correction of Publication

Accordingly, the notice of proposed rulemaking (REG–100908–23) that is the subject of FR Doc. 2023–18514, published on August 30, 2023, is corrected on page 60018, in the first column, by correcting the fifth line of the heading to read ''1545–BQ62''.

Oluwafunmilayo A. Taylor,

Section Chief, Publications and Regulations Section, Associate Chief Counsel, (Procedure and Administration).

[FR Doc. 2024–07723 Filed 4–10–24; 8:45 am]

BILLING CODE 4830–01–P