Albany, NY; to Boston, MA; excluding the airspace within Canada.

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J–38 [Amended]

From Duluth, MN; to Green Bay, WI.

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J–94 [Amended]

From Oakland, CA; Manteca, CA; INT Manteca 047° and Mustang, NV, 208° radials; to Mustang; Lovelock, NV; Battle Mountain, NV; Lucin, UT; Rock Springs, WY; Scottsbluff, NE; O'Neill, NE; Fort Dodge, IA; Dubuque, IA; Northbrook, IL; Pullman, MI; to Flint, MI. From London, ON, Canada; Buffalo, NY; Albany, NY; to Boston, MA; excluding the airspace within Canada.

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J–546 [Removed]

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J–551 [Removed]

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J–553 [Removed]

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Paragraph 6010 Domestic VOR Federal Airways

V–84 [Amended]

From Northbrook, IL; Pullman, MI; Lansing, MI; to Flint, MI. From London, ON, Canada; Buffalo, NY; Geneseo, NY; INT Geneseo 091° and Syracuse, NY, 240° radials; to Syracuse; excluding the airspace within Canada.

* * * * *

V–216 [Amended]

From Lamar, CO; Hill City, KS; Mankato, KS; Pawnee City, NE; Lamoni, IA; Ottumwa, IA; Iowa City, IA; INT Iowa City 062° and Janesville, WI, 240° radials; to Janesville.

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V–320 [Amended]

From Pellston, MI; Traverse City, MI; Mount Pleasant, MI; to Saginaw, MI.

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V–337 [Amended]

From INT Briggs, OH, 077° and Youngstown, OH, 177° radials; to Akron, OH. From Saginaw, MI; Mount Pleasant, MI; to White Cloud, MI.

* * * * *

Issued in Washington, DC, on February 10, 2014.

Ellen Crum,

Acting Manager, Airspace Policy & Regulations Group.

[FR Doc. 2014–03181 Filed 2–12–14; 8:45 am]

BILLING CODE 4910–13–P

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[Docket No. DEA–381]

Schedules of Controlled Substances: Placement of Suvorexant into Schedule IV

AGENCY: Drug Enforcement Administration, Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Drug Enforcement Administration (DEA) proposes to place the substance suvorexant ([(7*R*)-4-(5-chloro-1,3-benzoxazol-2-yl)-7-methyl-1,4-diazepan-1-yl][5-methyl-2-(2*H*-1,2,3-triazol-2-yl)phenyl]methanone), including its salts, isomers, and salts of isomers, into schedule IV of the Controlled Substances Act (CSA). This proposed scheduling action is pursuant to the CSA which requires that such actions be made on the record after opportunity for a hearing through formal rulemaking. If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions applicable to schedule IV controlled substances on persons who handle (manufacture, distribute, dispense, import, export, engage in research, conduct instructional activities, or possess), or propose to handle suvorexant.

DATES: Interested persons may file written comments on this proposal in accordance with 21 CFR 1308.43(g). Comments must be submitted electronically or postmarked on or before March 17, 2014. Commenters should be aware that the electronic Federal Docket Management System will not accept comments after midnight Eastern Time on the last day of the comment period.

Interested persons, defined as those ''adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811),'' 21 CFR 1300.01, may file a request for hearing or waiver of participation pursuant to 21 CFR 1308.44 and in accordance with 21 CFR 1316.45, 1316.47, 1316.48, or 1316.49, as applicable. Requests for hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing must be received on or before March 17, 2014.

ADDRESSES: To ensure proper handling of comments, please reference ''Docket No. DEA–381'' on all electronic and written correspondence. The DEA 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. Go to *www.regulations.gov* and follow the on-line instructions at that site for submitting comments. An electronic copy of this document and supplemental information to this proposed rule are also available at *www.regulations.gov* for easy reference. Paper comments that duplicate electronic submissions are not necessary. All comments submitted to *www.regulations.gov* will be posted for public review and are part of the official docket record. Should you, however, wish to submit written comments, in lieu of electronic comments, they should be sent via regular or express mail to: Drug Enforcement Administration, Attention: DEA Federal Register Representative/ODW, 8701 Morrissette Drive, Springfield, VA 22152. All requests for a hearing and waivers of participation must be sent to: Drug Enforcement Administration, Attention: Hearing Clerk/LJ, 8701 Morrissette Drive, Springfield, VA 22152.

FOR FURTHER INFORMATION CONTACT: Ruth A. Carter, Office of Diversion Control, Drug Enforcement Administration; Mailing Address: 8701 Morrissette Drive, Springfield, VA 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 and will be made available for public inspection online at *www.regulations.gov*. Such information includes personal identifying information (such as your name, address, etc.) voluntarily submitted by the commenter.

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. If a comment has so much confidential business information that it cannot be effectively redacted, all or part of that comment may not be made publicly available. Comments containing personal identifying information or confidential business information identified as directed above will be made publicly available in redacted form.

The Freedom of Information Act (FOIA) applies to all comments received. If you wish to personally inspect the comments and materials received or the supporting documentation the DEA used in preparing the proposed action, these materials will be available for public inspection by appointment. To arrange a viewing, please see the **FOR FURTHER INFORMATION CONTACT** paragraph above.

Request for Hearing, Notice of Appearance at Hearing, or Waiver of Participation in Hearing

Pursuant to the provisions of the CSA, 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. In accordance with 21 CFR 1308.44(a)–(c), requests for a hearing, notices of appearance, and waivers of an opportunity for a hearing or to participate in a hearing may be submitted only by interested persons, defined as those ''adversely affected or aggrieved by any rule or proposed rule issuable pursuant to section 201 of the Act (21 U.S.C. 811).'' 21 CFR 1300.01. Requests for hearing and notices of appearance 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 interest of the person in the proceeding and the objections or issues, if any, concerning which the person desires to be heard. Any waiver must conform to the requirements of 21 CFR 1308.44(c) and 1316.49, including 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 is 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 [Title 21] for the schedule in which such drug is to be placed. . . .'' Requests for a hearing, notices of appearance at a hearing, and waivers of an opportunity for a hearing or to participate in a hearing must be submitted to the DEA using the address information provided above.

Legal Authority

The DEA implements and enforces titles II and III of the Comprehensive Drug Abuse Prevention and Control Act of 1970, as amended. Titles II and III are referred to as the ''Controlled Substances Act'' and the ''Controlled Substances Import and Export Act,'' respectively, and are collectively referred to as the ''Controlled Substances Act'' or the ''CSA'' for the purpose of this action. 21 U.S.C. 801–971. The DEA publishes the implementing regulations for these statutes in title 21 of the Code of Federal Regulations (CFR), parts 1300 to 1321. The CSA and its implementing regulations are designed to prevent, detect, and eliminate the diversion of controlled substances and listed chemicals into the illicit market while providing for the legitimate medical, scientific, research, and industrial needs of the United States. Controlled substances have the potential for abuse and dependence and are controlled to protect the public health and safety.

Under the CSA, controlled substances are classified into one of five schedules based upon their potential for abuse, their currently accepted medical use, and the degree of dependence the substance may cause. 21 U.S.C. 812. The initial schedules of controlled substances established by Congress are found at 21 U.S.C. 812(c), and the current list of all scheduled substances is published at 21 CFR part 1308.

Pursuant to 21 U.S.C. 811(a)(1), the Attorney General may, by rule, ''add to such a schedule or transfer between such schedules any drug or other substance if he (A) finds that such drug or other substance has a potential for abuse, and (B) makes with respect to such drug or other substance the findings prescribed by [21 U.S.C. 812(b)] for the schedule in which such drug is to be placed. . . .'' Pursuant to 28 CFR 0.100(b), the Attorney General has delegated this scheduling authority to the Administrator of the DEA who has further delegated this authority to the Deputy Administrator of the DEA under 28 CFR 0.104.

The CSA provides that 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 Health and Human Services (HHS); or (3) on the petition of any interested party. 21 U.S.C. 811(a). If finalized, this action would impose the regulatory controls and administrative, civil, and criminal sanctions of schedule IV controlled substances for any person who handles suvorexant.

Background

Suvorexant ([(7*R*)-4-(5-chloro-1,3-benzoxazol-2-yl)-7-methyl-1,4-diazepan-1-yl][5-methyl-2-(2*H*-1,2,3-triazol-2-yl)phenyl]methanone), also known as MK–4305, is a new chemical entity developed for the treatment of insomnia. Suvorexant is a novel, first in class, orexin receptor antagonist with a mechanism of action distinct from any marketed drug. It acts via inhibition of the orexin 1 (OX1) and orexin 2 (OX2) receptors. In pharmacological activity studies, suvorexant functioned as an antagonist as demonstrated by its ability to block agonist-induced calcium (Ca^{2+}) release.

Proposed Determination to Schedule Suvorexant

Pursuant to 21 U.S.C. 811(a), proceedings to add a drug or substance to those controlled under the CSA may be initiated by request of the Secretary of the HHS.[1] On June 27, 2013, the HHS provided the DEA with a scientific and medical evaluation document prepared by the FDA entitled ''Basis for the Recommendation to Place Suvorexant in Schedule IV 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 suvorexant as a new drug, along with the HHS' recommendation to control suvorexant under schedule IV of the CSA.

In response, the DEA reviewed the scientific and medical evaluation and scheduling recommendation provided by the HHS, and all other relevant data, and completed its own eight-factor review document 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

[1] As set forth in a memorandum of understanding entered into by the HHS, 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 the NIDA. 50 FR 9518, Mar. 8, 1985. In addition, because the Secretary of the HHS has delegated to the Assistant Secretary for Health of the HHS the authority to make domestic drug scheduling recommendations, for purposes of this document, all subsequent references to ''Secretary'' have been replaced with ''Assistant Secretary.''

considered by the DEA in its proposed scheduling action. Please note that both the DEA and HHS analyses are available in their entirety under ''Supporting and Related Material'' in the public docket for this proposed rule at *www.regulations.gov*, under Docket Number ''DEA–381.'' Full analysis of, and citations to, the information referenced in the summary may also be found in the supporting and related material.

1. *The Drug's Actual or Relative Potential for Abuse:* Suvorexant is a new chemical entity that has not been marketed in the United States or any other country. As such, there is no information available detailing actual abuse of suvorexant. However, the legislative history of the CSA offers the following criterion for assessing a new drug or substance's potential for abuse:

> 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.[2]

As described further below, there is strong evidence that suvorexant produces behavioral effects in humans and in animals that are similar to those produced by zolpidem (schedule IV).

With a mechanism of action that is distinct from any other marketed drug, including those marketed for insomnia (i.e., schedule IV benzodiazepines, and non-benzodiazepine hypnotics such as zolpidem (schedule IV), eszopiclone [3] (schedule IV), and zaleplon (schedule IV)), suvorexant acts as an antagonist at the OX1 and OX2 receptors and produces sedative and sleep promoting effects in humans.

In a human abuse potential study in subjects with histories of recreational sedative use, suvorexant produced reinforcing subjective effects similar to zolpidem (schedule IV). Doses of 40, 80, and 150 mg of suvorexant were compared to 15 and 30 mg doses of zolpidem (schedule IV). On the visual analog scale (VAS), suvorexant produced '' 'at the moment' Drug Liking'' and ''High and Good,'' effects statistically indistinguishable from zolpidem (schedule IV). Suvorexant also produced effects similar to zolpidem (schedule IV) in ''Overall Drug Liking,'' ''Take Drug Again,'' ''Any Drug Effect,'' assessments of subjective drug value, and overall familiarity measures. Additionally, on the Bowdle VAS (a measure of perceptual and hallucinogenic effects) suvorexant produced effects statistically similar to zolpidem (schedule IV). Suvorexant produced less dysphoria and adverse effects than zolpidem (schedule IV), suggesting that suvorexant may have an increased abuse potential relative to zolpidem (schedule IV). Measures to evaluate cognitive and psychomotor impairment (e.g., reaction time, attention, and vigilance) showed that suvorexant produced levels of impairment that were similar to the low dose (15 mg) of zolpidem (schedule IV). These data suggest that zolpidem (schedule IV) and suvorexant present a similar risk to the public health, and that suvorexant impairs cognition at both therapeutic (e.g., 40 mg) and supratherapeutic doses. As the dose of suvorexant increased, there was no increase in drug effects. This fact is especially important because the lowest dose of suvorexant examined in the human abuse potential study (40 mg) is the maximum planned therapeutic dose—suggesting that therapeutic doses of suvorexant (e.g., 40 mg) will have significant abuse liability and produce cognitive and psychomotor impairment.

These data suggest that suvorexant and zolpidem (schedule IV) have a similar abuse potential. The similarities between suvorexant and zolpidem (schedule IV) indicate that there will be significant diversion of these substances from legitimate channels, and significant use contrary to or without medical advice. In addition, as discussed in Factor 3, the long half-life of suvorexant may be a critical factor in the drug's safety profile as suvorexant's duration of action may create significant hazards to the health of the user or to the safety of the community, and result in ''next day'' effects in patients.

2. *Scientific Evidence of the Drug's Pharmacological Effects, if Known:* The orexin signaling system was discovered in 1998 and has been implicated in numerous physiological functions involving the central nervous system (CNS) such as sleep and wakefulness, appetite/metabolism, stress response, reward/addiction, and analgesia. Orexin A and orexin B are peptide neurotransmitters produced through cleavage of a preprohormone. These neurotransmitters bind with a high degree of selectivity to two different G-protein coupled receptors (GPCR's), namely OX1 and OX2. These orexin receptors are broadly expressed in cortical, thalamic, and hypothalamic neuronal circuits. Suvorexant blocks the wakefulness promoting effects of the orexins, facilitating the sleep process. In pharmacological studies, suvorexant functioned as an antagonist as demonstrated by its ability to block agonist-induced calcium (Ca^{2+}) release.

In receptor binding studies to determine the binding affinity as assessed by the ability of suvorexant to displace a reference compound (expressed as K_i value), suvorexant produced K_i values of 0.55 nM and 0.35 nM for the OX1 and OX2 receptors, indicating a high affinity for these receptor subtypes. In *in vitro* functional studies, suvorexant blocked the effects of orexin receptor agonist in cells expressing OX1 and OX2 receptors. The concentrations of suvorexant inhibiting 50 percent of response (known as IC_{50}) were 49.9 nM at the OX1 receptors and 54.8 nM at OX2 receptors.

Like zolpidem, suvorexant (10, 20, 30 and 60 mg/kg) dose dependently reduced locomotor activity in rats, an expected characteristic of a sedative drug. Although rhesus monkeys trained to self-administer methohexital (schedule IV) did not self-administer suvorexant, the predictive validity of self-administration studies in evaluating the abuse potential of drugs acting via orexin receptors is unknown.

A human abuse potential study was performed to assess the abuse potential of suvorexant in human participants. The study demonstrated that suvorexant and zolpidem (schedule IV) produce similar reinforcing effects and have a similar potential for abuse in recreational drug users. Results showed that suvorexant produced effects statistically indistinguishable from zolpidem (schedule IV) in primary and secondary outcome measures. There was no increase in drug effects as the dose of suvorexant increased. This is an important observation, as the low dose of suvorexant (40 mg) in the human abuse potential study is the maximum proposed therapeutic dose. These data suggest that the maximum therapeutic dose of suvorexant (40 mg) was shown to produce cognitive and psychomotor impairment and will have a significant liability for abuse.

Results from another study measuring the effects of suvorexant (10, 50, and 100 mg) on sleep parameters and next-day residual effects demonstrated that the mid and high doses of suvorexant (50 and 100 mg) produced effects on next-day assessments of psychomotor performance and subjective effects. These results may be clinically relevant

[2] Comprehensive Drug Abuse Prevention and Control Act of 1970, H.R. Rep. No. 91–1444, 91st Cong., Sess. 1 (1970); *as reprinted in* 1970 U.S.C.C.A.N. 4566, 4601.

[3] Eszopiclone is the dextrarotory stereoisomer, i.e., an isomer, of zopiclone (schedule IV).

as the residual effects may be present in the morning following an evening administration (10 hours post-dose).

3. *The State of Current Scientific Knowledge Regarding the Drug or Other Substance:* The chemical name for suvorexant is [(7*R*)-4-(5-chloro-1,3-benzoxazol-2-yl)-7-methyl-1,4-diazepan-1-yl][5-methyl-2-(2*H*-1,2,3-triazol-2-yl)phenyl]methanone. It is a white to off-white powder. Other chemical names include: 1) Methanone, [(7*R*)-4-(5-chloro-2-benzoxazolyl)hexahydro-7-methyl-1*H*-1,4-diazepin-1-yl][5-methyl-2-(2*H*-1,2,3-triazol-2-yl)phenyl]-; 2) [(7*R*)-4-(5-chlorobenzoxazol-2-yl)-7-methylhexahydro-1*H*-1,4-diazepin-1-yl][5-methyl-2-(2*H*-1,2,3-triazol-2-yl)phenyl]methanone; 3) MK–4305; and 4) DORA–22. The Chemical Abstract Services number (CAS #) of suvorexant is: 1030377–33–3. At 25 °C, suvorexant is insoluble in water, soluble in methanol, very slightly soluble in heptane, and soluble in isopropyl acetate. The pH of a saturated aqueous solution of suvorexant was 8.6. Suvorexant has a molecular formula of $C_{23}H_{23}ClN_6O_2$ and a molecular weight of 450.921 g. Suvorexant has a distinct chemical structure that is different from that of other sedative hypnotics such as the benzodiazepines (schedule IV).

There are several metabolites of suvorexant, although none appear to contribute significantly to its pharmacodynamic effects or abuse potential. Eight metabolites were detected in the plasma of healthy males administered radiolabeled suvorexant, with two of the metabolites present at concentrations great than 10 percent (M9 and M12). After oral administration of 15–40-mg, peak plasma concentrations (i.e., T_{max}) of suvorexant occurred at approximately 1–2 hours (range 0.5–6.0 hours), although the study authors noted slight variability based on the time of day. The terminal half-life of suvorexant is approximately 8–11 hours after a 40-mg dose. The pharmacokinetics of suvorexant following multiple dose administrations were similar to those following single dose administrations, with slightly less than dose proportional pharmacokinetics over 10–80 mg as assessed by $AUC_{0-\infty}$ and C_{max}. Steady state exposure was reached after 2–3 days of consecutive dosing.

4. *Its History and Current Pattern of Abuse:* Suvorexant is not currently marketed or available for sale in any country, therefore there is no known history or pattern of abuse. However, results from the human abuse potential study suggest that suvorexant produces effects that are similar to zolpidem (schedule IV) and would have a similar pattern of abuse.

5. *The Scope, Duration, and Significance of Abuse:* While the current scope, duration, and significance of abuse of suvorexant are unknown due to its non-marketed status, the results of the human abuse potential study previously described suggest that, upon marketing, the scope, duration, and significance of suvorexant abuse may be similar to zolpidem (schedule IV). Data from the Drug Abuse Warning Network (DAWN) and the Adverse Event Reporting System (AERS) demonstrate the scope, duration, and significance of abuse of zolpidem (schedule IV) and related sedative-like drugs. In general, emergency department (ED) visits reported for zolpidem (schedule IV) along with those specifically categorized as ''misuse/abuse'' have increased every year from 2004 to 2010, with a modest decrease reported for 2011. ED visits related to benzodiazepine sedatives including diazepam (schedule IV) and lorazepam (schedule IV) demonstrated a similar trend. Suvorexant would be expected to have a similar scope, duration, and significance of abuse.

6. *What, If Any, Risk There Is to the Public Health:* Suvorexant has a long terminal half-life of approximately 8–11 hours, which may increase the duration of its sedative effects and psychomotor impairment. Suvorexant's extended duration of action increases its risk to the public health relative to zolpidem (schedule IV) and other short acting sedatives. Results of the human abuse potential study showed that suvorexant produces behavioral impairment, as evidenced by its effects on psychomotor performance and cognitive function. On these assessments, suvorexant generally produced deficits that were statistically indistinguishable from 15 mg of zolpidem (schedule IV), demonstrating the behavioral impairing effects of suvorexant, and suggesting that even at therapeutic doses, suvorexant will present a risk to the public health that is at least equivalent to that of zolpidem (schedule IV).

7. *Its Psychic or Physiological Dependence Liability:* Results of the human abuse potential study demonstrate that suvorexant has a psychic dependence liability similar to zolpidem (schedule IV). Self-administration in laboratory animals, epidemiological data documenting its use and abuse, and the ability to produce ''Drug Liking'' in human drug users demonstrate the psychic dependence liability of zolpidem (schedule IV). Similar data was collected for suvorexant and compared to zolpidem.

Discontinuation studies suggest that suvorexant does not produce physical dependence or withdrawal syndrome. Observed effects following suvorexant discontinuation include the return of insomnia symptoms. Furthermore, a lack of tolerance in humans from suvorexant was demonstrated by the sustained efficacy of suvorexant in Phase 3 trials where subjects reported improvement in sleep-related assessments that were still present one month after the start of treatment.

8. *Whether the Substance is an Immediate Precursor of a Substance Already Controlled under the CSA:* Suvorexant is not an immediate precursor of a substance already controlled under the CSA.

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

Proposed 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 the HHS and review of all available data, the Deputy Administrator of the DEA, pursuant to 21 U.S.C. 812(b)(4), finds that:

1. Suvorexant has a low potential for abuse relative to the drugs or other substances in schedule III. The overall abuse potential of suvorexant is comparable to schedule IV controlled substances such as zolpidem;

2. Upon approval of the pending new drug application, suvorexant will have a currently accepted medical use in the treatment of insomnia in the United States; and

3. The available evidence indicates that abuse of suvorexant may lead to limited psychological dependence relative to the drugs or other substances in schedule III. The potential for psychological dependence is similar to that of zolpidem (schedule IV).

Based on these findings, the Deputy Administrator of the DEA concludes that suvorexant ([(7*R*)-4-(5-chloro-1,3-benzoxazol-2-yl)-7-methyl-1,4-diazepan-1-yl][5-methyl-2-(2*H*-1,2,3-triazol-2-yl)phenyl]methanone), including its salts, isomers, and salts of isomers

warrants control in schedule IV of the CSA. 21 U.S.C. 812(b)(4).

Requirements for Handling Suvorexant

If this rule is finalized as proposed, suvorexant would be subject to the CSA's schedule IV 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:

Registration. Any person who handles (manufactures, distributes, dispenses, imports, exports, engages in research, or conducts instructional activities with) suvorexant, or who desires to handle suvorexant, would be 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. Any person who currently handles suvorexant, and is not registered with the DEA, would need to be registered with the DEA by the effective date of the final rule 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. Suvorexant would be subject to schedule III–V security requirements and would need to be handled and stored pursuant to 21 U.S.C. 821, 823, 871(b) and in accordance with 21 CFR 1301.71–1301.93.

Labeling and Packaging. All labels and labeling for commercial containers of suvorexant on or after finalization of this rule would need to comply with 21 U.S.C. 825, 958(e), and be in accordance with 21 CFR part 1302.

Inventory. Every DEA registrant who possesses any quantity of suvorexant on the effective date of the final rule would be required to take an inventory of all stocks of suvorexant on hand as of the effective date of the rule, pursuant to 21 U.S.C. 827, 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11(a) and (d).

Any person who becomes registered with the DEA after the effective date of the final rule would be required to take an initial inventory of all stocks of controlled substances (including suvorexant) on hand at the time of registration pursuant to 21 U.S.C. 827, 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11(a) and (b). After the initial inventory, every DEA registrant would be required to take a biennial inventory of all controlled substances (including suvorexant) on hand, on a biennial basis, pursuant to 21 U.S.C. 827, 958, and in accordance with 21 CFR 1304.03, 1304.04, and 1304.11.

Records. All DEA registrants would be required to maintain records with respect to suvorexant pursuant to 21 U.S.C. 827, 958, and in accordance with 21 CFR parts 1304, 1307, and 1312.

Prescriptions. All prescriptions for suvorexant or products containing suvorexant would need to comply with 21 U.S.C. 829, and be issued in accordance with 21 CFR part 1306, and part 1311 subpart C.

Importation and Exportation. All importation and exportation of suvorexant would need to be in compliance with 21 U.S.C. 952, 953, 957, and 958, and in accordance with 21 CFR part 1312.

Criminal Liability. Any activity involving suvorexant not authorized by, or in violation of, the CSA, occurring on or after finalization of this proposed rule, would be unlawful, and may subject the person to administrative, civil, and/or criminal sanctions.

Regulatory Analyses

Executive Orders 12866 and 13563

In accordance with 21 U.S.C. 811(a), this proposed 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 12866 and the principles reaffirmed in Executive Order 13563.

Executive Order 12988

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

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

This proposed rule will 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 Deputy Administrator, in accordance with the Regulatory Flexibility Act (RFA), 5 U.S.C. 601–612, 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. The purpose of this proposed rule is to place suvorexant, including its salts, isomers, and salts of isomers, into schedule IV of the CSA. No less restrictive measures (i.e., non-control, or control in schedule V) enable the DEA to meet its statutory obligations under the CSA. In preparing this certification, the DEA has assessed economic impact by size category and has considered costs with respect to the various DEA registrant business activity classes.

Suvorexant is a new molecular entity which has not yet been marketed in the United States or any other country. Accordingly, the number of currently identifiable manufacturers, importers, and distributors for suvorexant is extremely small. The publicly available materials also specify the readily identifiable persons subject to direct regulation by this proposed rule. Based on guidelines utilized by the Small Business Administration (SBA), the suvorexant manufacturer/distributor/importer was determined not to be a small entity. Once generic equivalents are developed and approved for manufacturing and marketing, there may be additional manufacturers, importers, and distributors of suvorexant, but whether they may qualify as small entities cannot be determined at this time.

There are approximately 1.5 million controlled substance registrants, who represent approximately 381,000 entities (which include businesses, organizations, and governmental jurisdictions). The DEA estimates that 371,000 (97 percent) of these entities are considered ''small entities'' in accordance with the RFA and SBA standards. 5 U.S.C. 601(6); 15 U.S.C. 632. Due to the wide variety of unidentifiable and unquantifiable variables that potentially could influence the dispensing rates of new molecular entities, the DEA is unable to determine what number of these 371,000 small entities might handle suvorexant.

Despite the fact that the number of small entities possibly impacted by this proposed rule could not be determined, the DEA concludes that they would not experience a significant economic impact as a result of this proposed rule. The DEA estimates all anticipated suvorexant handlers to be DEA registrants and currently 98 percent of DEA registrants (most of which are small entities) are authorized to handle schedule IV controlled substances. Even assuming that all of these registrants were to handle suvorexant the costs that they would incur as a result of suvorexant scheduling would be nominal as they have already established and implemented the required security, inventory, recordkeeping, and labeling systems and processes to handle schedule IV controlled substances.

Because of these facts, this proposed rule will not result in 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.,* 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 requirement 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 21 CFR part 1308 continues to read as follows:

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

■ 2. Amend § 1308.14 by redesignating paragraphs (c)(50) through (c)(55) as paragraphs (c)(51) through (c)(56) and adding new paragraph (c)(50) to read as follows:

§ 1308.14 Schedule IV.

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(c) * * *

(50) Suvorexant 2223

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Dated: February 7, 2014.

Thomas M. Harrigan,

Deputy Administrator.

[FR Doc. 2014–03124 Filed 2–12–14; 8:45 am]

BILLING CODE 4410–09–P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 50

[FRL–9906–45–ORD; Docket ID No. EPA–HQ–ORD–2013–0620 and Docket ID No. EPA–HQ–OAR–2014–0128]

Notice of Workshop in Support of the Review of the Secondary National Ambient Air Quality Standards for Oxides of Nitrogen and Sulfur

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of workshop.

SUMMARY: EPA is announcing a ''*Workshop to Discuss Policy-Relevant Science to Inform EPA's Review of the Secondary National Ambient Air Quality Standards (NAAQS) for Oxides of Nitrogen and Sulfur.*'' This workshop is being organized by EPA's Office of Research and Development's, National Center for Environmental Assessment (NCEA) and the Office of Air and Radiation's, Office of Air Quality Planning and Standards (OAQPS). The workshop will be held March 4–6, 2014, in Research Triangle Park, North Carolina, and it will be open to attendance by interested public observers on a first-come, first-served basis up to the limits of available space.

DATES: The workshop will be held March 4–6, 2014. The pre-registration deadline is February 28, 2014.

ADDRESSES: The workshop will be held at U.S. EPA, 109 T.W. Alexander Drive, Research Triangle Park, North Carolina. An EPA contractor, ICF International, is providing logistical support for the workshop. Please register by going to: *https://sites.google.com/site/soxnoxkickoffworkshop/.*

FOR FURTHER INFORMATION CONTACT: Please direct questions regarding workshop registration or logistics to Courtney Skuce at: *EPA_NAAQS_Workshop@icfi.com* or by phone at: 919–293–1660. For technical information, contact Tara Greaver, Ph.D., NCEA; telephone: 919–541–2435; or email: *greaver.tara@epa.gov* or Ginger Tennant, OAQPS; telephone: 919–541–4072; or email: *tennant.ginger@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. Information About the Workshop

Section 108(a) of the Clean Air Act directs the Administrator to issue ''air quality criteria'' for certain air pollutants. These air quality criteria are to ''accurately reflect the latest scientific knowledge useful in indicating the kind and extent of all identifiable effects on public health or welfare, which may be expected from the presence of such pollutant in the ambient air. . . .'' Under section 109 of the Act, EPA is then to establish National Ambient Air Quality Standards (NAAQS) for each pollutant for which EPA has issued criteria. Section 109(d) of the Act subsequently requires periodic review and, if appropriate, revision of existing air quality criteria to reflect advances in scientific knowledge on the effects of the pollutant on public health and welfare. EPA is also to revise the NAAQS, if appropriate, based on the revised air quality criteria.

NO_X and SO_X are two of six ''criteria'' pollutants for which EPA has established NAAQS. Periodically, EPA reviews the scientific basis for these standards by preparing an Integrated Science Assessment (ISA). The ISA, along with additional technical and policy assessments conducted by OAQPS, form the basis for EPA decisions on the adequacy of existing NAAQS and the appropriateness of new or revised standards.

This workshop is designed to inform the planning for EPA's recently initiated review of the secondary (welfare-based) NAAQS for Oxides of Nitrogen and Sulfur. The **Federal Register** notice issuing EPA's call for information for the recently initiated review is available at: *http://www.epa.gov/ttn/naaqs/standards/no2so2sec/2013_fr.html.* Consistent with the NAAQS review process, the workshop will provide an opportunity for those attending to highlight key science issues that they consider relevant to EPA's review of the standards (referred to as ''policy-