the individual ingredients differ, the directions for the combination product may not contain any dosage that exceeds those established for any individual ingredient in the applicable OTC drug monograph(s), and may not provide for use by any age group lower than the highest minimum age limit established for any individual ingredient.''

Concerns about effectiveness also stem from a study (Ref. 8) indicating that separate application of sunscreen followed by DEET resulted in a decrease in sun protection factor (SPF) after application of the insect repellent. Thus, FDA is soliciting comment on the following questions:

1. Is there additional evidence suggesting that application of a sunscreen product followed by application of a separate insect repellent product results in a decrease in the sunscreen's SPF? Is there evidence suggesting that sequential application of the products has no adverse effect on the sunscreen?

2. Is there evidence suggesting that combining a sunscreen and insect repellent in a single formulation adversely impacts the effectiveness of the sunscreen? Is there evidence suggesting that such a combination has no adverse impact on the sunscreen component?

3. Are there effective concentrations of the insect repellent ingredients that could be used to allow for liberal application and frequent reapplication of the insect repellent-sunscreen drug products, as directed by the sunscreen directions, without jeopardizing the safety of the consumer? How does this vary by insect repellent ingredient? Would any of the insect repellent ingredients be effective at such concentrations?

4. Is there information available to show whether there are any chemical or physical incompatibilities between insect repellent and sunscreen active ingredients when used in combination products or when used separately? Are there any sunscreen ingredients that should not be used with a specific insect repellent ingredient?

5. If an insect repellent ingredient (e.g., DEET) is labeled for 6-hour intervals between applications, can the effectiveness of the sunscreen be assured if the product cannot be applied more often than every 6 hours? Is there a need for a minimal SPF to assure the effectiveness of the combination product considering the wide variation in minimal erythemal dose (MED) between individuals and the need for reapplication due to physical stress such as toweling or rubbing of the skin? If the answer is yes, what minimal SPF value should be required, and what is the basis for that SPF value?

6. Is there information available to demonstrate that there are product performance benefits [other than the convenience of using one product instead of two] derived from the concurrent application of the insect repellent and the sunscreen (as opposed to sequential application of these products separately)? Please submit any data that you reference.

7. Oil of Citronella products are labeled to repeat applications at 1 hour intervals for maximum repellent effectiveness. Is it possible that insect repellent-sunscreen drug products can be formulated in such a way that the insect repellent reapplication intervals coincide more closely with the sunscreen reapplication intervals? Can this be done without jeopardizing the safety or effectiveness of these products?

III. Request for Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on this document. Three copies of all written comments are to be submitted. Individuals submitting written comments or anyone submitting electronic comments may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

IV. References

The following references are on display in the Division of Dockets Management (see **ADDRESSES**) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. EPA Reregistration Eligibility Decision for DEET, 1998.

2. EPA Reregistration Eligibility Decision for Oil of Citronella, 1997.

3. EPA Biopesticide Registration Eligibility Document for IR3535, 1999.

4. EPA Biopesticide Registration Eligibility Document for p-menthane-3,8-diol, 2000.

5. EPA Decision Memorandum on KBR 3023, 2000.

6. Ross, E. A. et al., ''Insect Repellent Interactions: Sunscreens Enhance DEET (*N,N*-Diethyl-*M*-Toluamide) Absorption,'' *Drug Metabolism and Disposition*, 32:783–785, 2004.

7. Gu, X. et al., ''In Vitro Evaluation of Concurrent Use of Commercially Available Insect Repellent and Sunscreen Preparations,'' *British Journal of Dermatology*, 152: 1263–1267, 2005.

8. Montemarano, A. D. et al., ''Insect Repellents and the Efficacy of Sunscreens,'' *The Lancet*, 349:1670–1671, 1997.

This request for information and comment is issued under sections 201, 501, 502, 503, 505, 510, and 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, and 371) and under authority of the Commissioner of Food and Drugs.

Dated: December 5, 2006.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. E7–2890 Filed 2–21–07; 8:45 am]

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DEPARTMENT OF JUSTICE

Drug Enforcement Administration

[Docket No. DEA–301P]

21 CFR Part 1308

Schedules of Controlled Substances: Placement of Lisdexamfetamine into Schedule II

AGENCY: Drug Enforcement Administration, U.S. Department of Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: This proposed rule is issued by the Deputy Administrator of the Drug Enforcement Administration (DEA) to place the substance lisdexamfetamine, including its salts, isomers, and salts of isomers, into schedule II of the Controlled Substances Act (CSA). This proposed action is based on a recommendation from the Assistant Secretary for Health of the Department of Health and Human Services (DHHS) and on an evaluation of the relevant data by DEA. This scheduling of lisdexamfetamine in schedule II will not be finalized until a New Drug Application (NDA) for a lisdexamfetamine product is approved by the Food and Drug Administration (FDA). If finalized, this action would impose the regulatory controls and criminal sanctions of schedule II on those who handle lisdexamfetamine and products containing lisdexamfetamine.

DATES: Written comments must be postmarked, and electronic comments must be sent, on or before March 26, 2007.

ADDRESSES: To ensure proper handling of comments, please reference ''Docket No. DEA–301'' on all written and electronic correspondence. Written comments sent via regular mail should be sent to the Deputy Administrator, Drug Enforcement Administration, Washington, DC 20537, Attention: DEA

Federal Register Representative/ODL. Written comments sent via express mail should be sent to the Deputy Administrator, Drug Enforcement Administration, Attention: DEA Federal Register Representative/ODL, 2401 Jefferson-Davis Highway, Alexandria, VA 22301. Comments may be directly sent to DEA electronically by sending an electronic message to *dea.diversion.policy@usdoj.gov.* Comments may also be sent electronically through *http://www.regulations.gov* using the electronic comment form provided on that site. An electronic copy of this document is also available at the *http://www.regulations.gov* Web site. DEA will accept electronic comments containing MS Word, WordPerfect, Adobe PDF, or Excel file formats only. DEA will not accept any file format other than those specifically listed here.

FOR FURTHER INFORMATION CONTACT: Christine Sannerud, PhD, Chief, Drug and Chemical Evaluation Section, Drug Enforcement Administration, Washington, DC 20537, (202) 307–7183.

SUPPLEMENTARY INFORMATION: Lisdexamfetamine is a central nervous system stimulant drug. The Food and Drug Administration (FDA) is currently reviewing a New Drug Application (NDA) for lisdexamfetamine. Upon approval of this pending NDA, lisdexamfetamine will be marketed as a prescription drug product for the treatment of Attention Deficit Hyperactivity Disorder (ADHD).

Lisdexamfetamine is an amide ester conjugate comprised of the amino acid L-lysine covalently bound to the amino group of d-amphetamine. The chemical name of its dimesylate salt form is (2S)-2,6-diamino-N-[(1S)-1-methyl-2-phenethyl]hexanamide dimethanesulfonate (CAS number 608137–32–3). Lisdexamfetamine per se is pharmacologically inactive and its effects are due to its in vivo metabolic conversion to d-amphetamine. In this regard, lisdexamfetamine acts as a prodrug.

Lisdexamfetamine shares substantial pharmacological effects and abuse potential with amphetamine. Lisdexamfetamine is positively reinforcing in monkeys. It generalizes to the discriminative stimulus effects of d-amphetamine in monkeys. It produces locomotor stimulation in rats. In adults, the total amphetamine exposure resulting from 75 mg oral lisdexamfetamine is equivalent to 35 mg oral Adderall XR, an extended release amphetamine product. Peak plasma concentrations of d-amphetamine following oral ingestion of 50 and 70 mg lisdexamfetamine correspond closely to those produced by oral ingestion of 30 and 50 mg immediate-release d-amphetamine product. In controlled clinical studies, lisdexamfetamine has been found to be similar to d-amphetamine in psychoactive measures. It produces euphoria in humans typical of d-amphetamine. Lisdexamfetamine shows an adverse event profile similar to that of d-amphetamine. Some adverse effects of lisdexamfetamine include insomnia, nervousness, irritability, anorexia, weight loss, mood alterations, and increases in blood pressure and heart rate.

Lisdexamfetamine has not been studied for its psychological and physical dependence potential. However, since lisdexamfetamine is a prodrug for d-amphetamine, it is expected to possess dependence potential similar to that of d-amphetamine. d-Amphetamine is known to cause both psychological and physical dependence. Some symptoms of d-amphetamine withdrawal include depression, increase in sleep and food intake, drug craving, anhedonia, irritability and poor concentration.

Lisdexamfetamine is a new molecular entity and has not been marketed in the United States or other countries. Therefore, there has been no evidence of diversion, abuse, or law enforcement encounters involving lisdexamfetamine. On November 14, 2006, the Assistant Secretary for Health, DHHS, sent the Deputy Administrator of DEA a scientific and medical evaluation and a letter recommending that lisdexamfetamine be placed into schedule II of the CSA. Enclosed with the November 14, 2006 letter was a document prepared by the FDA entitled, ''Basis for the Recommendation for Control of Lisdexamfetamine in Schedule II of the Controlled Substances Act.'' The document contained a review of the factors which the CSA requires the Secretary to consider (21 U.S.C. 811(b)).

The factors considered by the Assistant Secretary of Health and DEA with respect to lisdexamfetamine were:

(1) Its actual or relative potential for abuse;

(2) Scientific evidence of its pharmacological effects;

(3) The state of current scientific knowledge regarding the drug;

(4) Its history and current pattern of abuse;

(5) The scope, duration, and significance of abuse;

(6) What, if any, risk there is to the public health;

(7) Its psychic or physiological dependence liability; and

(8) Whether the substance is an immediate precursor of a substance already controlled under this subchapter. (21 U.S.C. 811(c))

Based on the recommendation of the Assistant Secretary for Health, received in accordance with section 201(b) of the Act (21 U.S.C. 811(b)), and the independent review of the available data by DEA, the Deputy Administrator of DEA, pursuant to sections 201(a) and 201(b) of the Act (21 U.S.C. 811(a) and 811(b)), finds that:

(1) Lisdexamfetamine has a high potential for abuse;

(2) Upon approval of the pending NDA, lisdexamfetamine will have a currently accepted medical use in treatment in the United States; and

(3) Abuse of lisdexamfetamine may lead to severe psychological or physical dependence.

Based on these findings, the Deputy Administrator of DEA concludes that lisdexamfetamine, including its salts, isomers, and salts of isomers, warrants control in schedule II of the CSA, if and when an NDA for lisdexamfetamine is approved.

Interested persons are invited to submit their comments, objections or requests for a hearing with regard to this proposal. Requests for a hearing should state, with particularity, the issues concerning which the person desires to be heard. All correspondence regarding this matter should be submitted to the Deputy Administrator, Drug Enforcement Administration, Washington, DC, 20537, Attention: DEA Federal Register Representative/ODL. In the event that comments, objections, or requests for a hearing raise one or more issues which the Deputy Administrator finds warrant a hearing, the Deputy Administrator shall order a public hearing by notice in the **Federal Register**, summarizing the issues to be heard and setting the time for the hearing.

Requirements for Handling Lisdexamfetamine

If this rule is finalized as proposed, lisdexamfetamine would be subject to CSA regulatory controls and administrative, civil and criminal sanctions applicable to the manufacture, distribution, dispensing, importing and exporting of a schedule II controlled substance, including the following:

Registration. Any person who manufactures, distributes, dispenses, imports, exports, engages in research or conducts instructional activities with lisdexamfetamine, or who desires to manufacture, distribute, dispense, import, export, engage in instructional activities or conduct research with

lisdexamfetamine, would be required to be registered to conduct such activities in accordance with Part 1301 of Title 21 of the Code of Federal Regulations.

Security. Lisdexamfetamine would be subject to schedule II security requirements and must be manufactured, distributed and stored in accordance with §§ 1301.71, 1301.72(a), (c), and (d), 1301.73, 1301.74, 1301.75(b) and (c), 1301.76 and 1301.77 of Title 21 of the Code of Federal Regulations.

Labeling and Packaging. All labels and labeling for commercial containers of lisdexamfetamine which are distributed after finalization of this rule would be required to comply with requirements of §§ 1302.03–1302.07 of Title 21 of the Code of Federal Regulations.

Quotas. Quotas for lisdexamfetamine would be established pursuant to part 1303 of Title 21 of the Code of Federal Regulations.

Inventory. Every registrant required to keep records and who possesses any quantity of lisdexamfetamine would be required to keep an inventory of all stocks of lisdexamfetamine on hand pursuant to §§ 1304.03, 1304.04 and 1304.11 of Title 21 of the Code of Federal Regulations. Every registrant who desires registration in schedule II for lisdexamfetamine would be required to conduct an inventory of all stocks of the substance on hand at the time of registration.

Records. All registrants would be required to keep records pursuant to §§ 1304.03, 1304.04, 1304.21, 1304.22, and 1304.23 of Title 21 of the Code of Federal Regulations.

Reports. All registrants required to submit reports to the Automation of Reports and Consolidated Order System (ARCOS) in accordance with § 1304.33 of Title 21 of the Code of Federal Regulations would be required to do so for lisdexamfetamine.

Orders for Lisdexamfetamine. All registrants involved in the distribution of lisdexamfetamine would be required to comply with the order form requirements of part 1305 of Title 21 of the Code of Federal Regulations.

Prescriptions. All prescriptions for lisdexamfetamine or prescriptions for products containing lisdexamfetamine would be required to be issued pursuant to 21 CFR 1306.03–1306.06 and 1306.11–1306.15.

Importation and Exportation. All importation and exportation of lisdexamfetamine would need to be in compliance with part 1312 of Title 21 of the Code of Federal Regulations.

Criminal Liability. Any activity with lisdexamfetamine not authorized by, or in violation of, the Controlled Substances Act or the Controlled Substances Import and Export Act occurring on or after finalization of this proposed rule would be unlawful.

Regulatory Certifications

Executive Order 12866

In accordance with 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 5 U.S.C. 556 and 557 and, as such, are exempt from review by the Office of Management and Budget pursuant to Executive Order 12866, section 3(d)(1).

Regulatory Flexibility Act

The Deputy Administrator, in accordance with the Regulatory Flexibility Act (5 U.S.C. 605(b)), 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. Lisdexamfetamine products will be prescription drugs used for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). Handlers of lisdexamfetamine will also handle other controlled substances used to treat ADHD which are already subject to the regulatory requirements of the CSA.

Executive Order 12988

This regulation meets the applicable standards set forth in Sections 3(a) and 3(b)(2) of Executive Order 12988 Civil Justice Reform.

Executive Order 13132

This rulemaking does not preempt or modify any provision of state law; nor does it impose enforcement responsibilities on any state; nor does it diminish the power of any state to enforce its own laws. Accordingly, this rulemaking does not have federalism implications warranting the application of Executive Order 13132.

Unfunded Mandates Reform Act of 1995

This rule will not result in the expenditure by state, local and tribal governments, in the aggregate, or by the private sector, of $118,000,000 or more in any one year, and will not significantly or uniquely affect small governments. Therefore, no actions were deemed necessary under provisions of the Unfunded Mandates Reform Act of 1995.

Congressional Review Act

This rule is not a major rule as defined by § 804 of the Small Business Regulatory Enforcement Fairness Act of 1996 (Congressional Review Act). This rule will not result in an annual effect on the economy of $100,000,000 or more; a major increase in costs or prices; or significant adverse effects on competition, employment, investment, productivity, innovation, or on the ability of United States-based companies to compete with foreign based companies in domestic and export markets.

List of Subjects in 21 CFR Part 1308

Administrative practice and procedure, Drug traffic control, Narcotics, Prescription drugs.

Under the authority vested in the Attorney General by section 201(a) of the CSA (21 U.S.C. 811(a)), and delegated to the Administrator of DEA by U.S. Department of Justice regulations (28 CFR 0.100), and redelegated to the Deputy Administrator pursuant to 28 CFR 0.104, the Deputy Administrator hereby proposes that 21 CFR part 1308 be amended as follows:

PART 1308—SCHEDULES OF CONTROLLED SUBSTANCES [AMENDED]

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. Section 1308.12 is proposed to be amended by adding a new paragraph (d)(5) to read as follows:

§ 1308.12 Schedule II.

* * * * *

(d) * * *

(5) Lisdexamfetamine, its salts, isomers, and salts of its isomers 1205

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Dated: February 12, 2007.

Michele M. Leonhart,

Deputy Administrator.

[FR Doc. E7–2993 Filed 2–21–07; 8:45 am]

BILLING CODE 4410–09–P