

## DEPARTMENT OF JUSTICE

## Drug Enforcement Administration

## 21 CFR Part 1308

[Docket No. DEA-319P]

**Schedules of Controlled Substances:  
Placement of Tapentadol Into Schedule II****AGENCY:** Drug Enforcement Administration, 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 tapentadol, including its isomers, esters, ethers, salts and salts of isomers, esters, and ethers whenever the existence of such isomers, esters, ethers, and salts is possible, 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. If finalized, this action would impose the regulatory controls and criminal sanctions of schedule II on those who handle tapentadol and products containing tapentadol.

**DATES:** Written comments must be postmarked on or before March 19, 2009, and electronic comments must be sent on or before midnight Eastern time March 19, 2009.

**ADDRESSES:** To ensure proper handling of comments, please reference "Docket No. DEA-319" on all written and electronic correspondence. Written comments sent via regular or express mail should be sent to the Drug Enforcement Administration, Attention: DEA Federal Register Representative/ODL, 8701 Morrisette Drive, Springfield, Virginia 22152. Comments may be sent to DEA by sending an electronic message to [dea.diversion.policy@usdoj.gov](mailto: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.

Please note that DEA is requesting that electronic comments be submitted before midnight Eastern time on the day

the comment period closes because <http://www.regulations.gov> terminates the public's ability to submit comments at midnight Eastern time on the day the comment period closes. Commenters in time zones other than Eastern time may want to consider this so that their electronic comments are received. All comments sent via regular or express mail will be considered timely if postmarked on the day the comment period closes.

**FOR FURTHER INFORMATION CONTACT:** Christine A. Sannerud, Ph.D., Chief, Drug and Chemical Evaluation Section, Drug Enforcement Administration, 8701 Morrisette Drive, Springfield, Virginia 22152, Telephone: (202) 307-7183.

**SUPPLEMENTARY INFORMATION:**

*Posting of Public Comments:* Please note that all comments received are considered part of the public record and made available for public inspection online at <http://www.regulations.gov> and in the Drug Enforcement Administration's public docket. 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 posted online or made available in the public docket, you must include the phrase "PERSONAL IDENTIFYING INFORMATION" in the first paragraph of your comment. You must also place all the personal identifying information you do not want posted online or made available in the public docket 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 posted online or made available in the public docket, you must include the phrase "CONFIDENTIAL BUSINESS INFORMATION" in the first paragraph of your comment. You must also prominently identify confidential business information to be redacted within the comment. If a comment has so much confidential business information that it cannot be effectively redacted, all or part of that comment may not be posted online or made available in the public docket.

Personal identifying information and confidential business information identified and located as set forth above will be redacted and the comment, in redacted form, will be posted online and placed in the DEA's public docket file.

Please note that the Freedom of Information Act applies to all comments

received. If you wish to inspect the agency's public docket file in person by appointment, please see the **FOR FURTHER INFORMATION CONTACT** paragraph.

**Background**

On November 20, 2008, the Food and Drug Administration (FDA) approved tapentadol for marketing in the United States as a prescription drug product for the treatment of moderate-to-severe acute pain. Tapentadol is a new molecular entity with centrally-acting analgesic properties.

Tapentadol has dual modes of action namely, mu ( $\mu$ ) opioid receptor agonistic action and inhibition of reuptake of norepinephrine at the norepinephrine transporter. The chemical name of its monohydrochloride salt form is 3-[(1R,2R)-3-(dimethylamino)-1-ethyl-2-methylpropyl]phenol hydrochloride.

Tapentadol shares substantial pharmacological effects and abuse potential with other schedule II opioid analgesics, e.g., morphine, oxycodone, and hydromorphone. Tapentadol has rewarding and reinforcing effects similar to those of morphine in animal models. It generalizes to the discriminative stimulus effects of morphine in rats and monkeys. Tapentadol, similar to morphine, produced conditioned place preference in rats, and this effect was antagonized by naloxone (an opioid receptor antagonist). In a clinical study with opioid-experienced non-dependent subjects, the subjective scores for drug liking of a single dose of tapentadol (50, 100 and 200 mg) were comparable to equianalgesic doses of hydromorphone (4, 8, and 16 mg). In clinical studies, tapentadol showed an adverse event profile similar to other schedule II opioids. The most commonly reported adverse events are nausea, dizziness, vomiting, somnolence, vertigo, and headache. In a clinical study in which the patients received equianalgesic doses of tapentadol or oxycodone for 90 days, the reports of withdrawal symptoms were comparable for both treatment groups upon discontinuance of administration. The ability of tapentadol to produce psychological dependence is suggested by a level of drug liking comparable to that produced by hydromorphone.

Since tapentadol is a new molecular entity, there has been no evidence of diversion, abuse, or law enforcement encounters involving the drug. On November 13, 2008, the Assistant Secretary for Health, DHHS, sent the Deputy Administrator of DEA a scientific and medical evaluation and a letter recommending that tapentadol be

placed into schedule II of the CSA. Enclosed with the November 13, 2008, letter was a document prepared by the FDA entitled, "Basis for the Recommendation for Control of Tapentadol 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 the DEA with respect to tapentadol 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 § 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 §§ 201(a) and 201(b) of the Act (21 U.S.C. 811(a) and 811(b)), finds that:

- (1) Tapentadol has a high potential for abuse;
- (2) Tapentadol currently has accepted medical use in treatment in the United States; and
- (3) Abuse of tapentadol may lead to severe psychological or physical dependence.

Based on these findings, the Deputy Administrator of DEA concludes that tapentadol, including its isomers, esters, ethers, salts and salts of isomers, esters, and ethers whenever the existence of such isomers, esters, ethers, and salts is possible, warrants control in schedule II of the CSA. (21 U.S.C. 812 (b)(2))

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 DEA to the address provided above. 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 Tapentadol**

If this rule is finalized as proposed, tapentadol would be subject to the 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 tapentadol, or who desires to manufacture, distribute, dispense, import, export, engage in instructional activities or conduct research with tapentadol, would be required to be registered to conduct such activities in accordance with Part 1301 of Title 21 of the Code of Federal Regulations (CFR).

**Security.** Tapentadol 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 CFR.

**Labeling and Packaging.** All labels and labeling for commercial containers of tapentadol 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 CFR.

**Quotas.** Quotas for tapentadol would be established pursuant to part 1303 of Title 21 of the CFR.

**Inventory.** Every registrant required to keep records and who possesses any quantity of tapentadol would be required to keep an inventory of all stocks of tapentadol on hand pursuant to §§ 1304.03, 1304.04 and 1304.11 of Title 21 of the CFR. Every registrant who desires registration in schedule II for tapentadol 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 CFR.

**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 CFR would be required to do so for tapentadol.

**Orders for tapentadol.** All registrants involved in the distribution of tapentadol would be required to comply

with the order form requirements of part 1305 of Title 21 of the CFR.

**Prescriptions.** All prescriptions for tapentadol or prescriptions for products containing tapentadol 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 tapentadol would need to be in compliance with part 1312 of Title 21 of the CFR.

**Criminal Liability.** Any activity with tapentadol not authorized by, or in violation of, the CSA 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. 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. Tapentadol products will be prescription drugs used for the treatment of moderate-to-severe acute pain. Handlers of tapentadol will also handle other controlled substances used to treat pain which are already subject to the regulatory requirements of the CSA.

##### *Executive Order 12988*

This regulation meets the applicable standards set forth in §§ 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 \$120,000,000 or more (adjusted for inflation) 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 § 201(a) of the CSA (21 U.S.C. 811(a)), and delegated to the Administrator of the DEA by the 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**

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 amended in the table by adding a new paragraph (c)(28) to read as follows:

**§ 1308.12 Schedule II.**

\* \* \* \* \*

(c) \* \* \*

(28) Tapentadol 9780

\* \* \* \* \*

Dated: January 27, 2009.

**Michele M. Leonhart,**  
*Deputy Administrator.*

[FR Doc. E9-3150 Filed 2-13-09; 8:45 am]

**BILLING CODE 4410-09-P**

**DEPARTMENT OF TRANSPORTATION****Federal Transit Administration****49 CFR Part 611**

[Docket No. FTA-2006-25737]

RIN 2132-AA81

**Major Capital Investment Projects**

**AGENCY:** Federal Transit Administration (FTA), DOT.

**ACTION:** Notice of proposed rulemaking; withdrawal.

**SUMMARY:** This action withdraws a notice of proposed rulemaking (NPRM) concerning major capital investment projects published in the **Federal Register** on August 3, 2007 (72 FR 43328). FTA has determined that withdrawal of the NPRM is warranted due to an intervening statutory change.

**FOR FURTHER INFORMATION CONTACT:**

Christopher Van Wyk, Office of Chief Counsel, Federal Transit Administration, 1200 New Jersey Ave., SE., East Building, Fifth Floor, Washington, DC 20590, (202) 366-4011 or *Christopher.VanWyk@dot.gov*.

**SUPPLEMENTARY INFORMATION:****Background**

On August 10, 2005, President Bush signed the Safe, Accountable, Flexible, and Efficient Transportation Equity Act—A Legacy for Users (SAFETEA-LU). Section 3011 of SAFETEA-LU made a number of changes to 49 U.S.C. 5309, which authorizes the Federal Transit Administration's (FTA) capital investment grant program. SAFETEA-LU also required that FTA issue regulations establishing an evaluation and rating process for the new Small Starts program. To effectuate the statutory changes and comply with the rulemaking requirement, FTA published an advance notice of proposed rulemaking on January 30, 2006 and a notice of proposed rulemaking (NPRM) on August 3, 2007. On June 6, 2008, the SAFETEA-LU Technical Corrections Act of 2008 (122 Stat. 1572) was signed into law, amending 49 U.S.C. 5309 to require that FTA "give comparable, but not necessarily equal, numerical weight to each project justification criteria in calculating the overall project rating" for both New Start and Small Start projects. The revisions to the statute require such a fundamental change in how FTA weighs the several project justification criteria that a new approach to rulemaking for the New Starts and Small Starts program is required. Thus, FTA is publishing this notice to

withdraw the NPRM it issued on August 3, 2007.

FTA received numerous written comments in response to the NPRM. The majority of commenters opposed the NPRM, with overwhelmingly negative comment on a number of specific proposals. The following concerns emerged as the most widely held: A regulatory requirement that a project be rated medium on cost-effectiveness in order to obtain a funding recommendation; cost-effectiveness weighted fifty percent of the overall project justification rating; modification of the definition of "fixed guideway" to include High Occupancy Toll (HOT) lanes under certain conditions; consideration given to congestion reduction in evaluating projects; inclusion of weights for evaluation criteria in the regulatory text rather than in policy guidance; the level of simplification for the new Small Starts program; the combination of the evaluation measures for economic development and land use and the weight given to the combined measure; the prohibition on segmenting a New Starts project into several Small Starts projects; and the proposal for the Very Small Starts category of projects.

Today's issue of the **Federal Register** contains another withdrawal notice by which FTA is also withdrawing the NPRM it issued for the Contractor Performance Incentives for the Capital Investment Program on February 19, 2008 (73 FR 9075).

**The Withdrawal**

In consideration of the foregoing, the NPRM for FTA Docket No. FTA-2006-25737, as published in the **Federal Register** on August 3, 2007 (72 FR 43328) is hereby withdrawn.

Issued in Washington, DC, this 10th day of February, 2009.

**Matthew J. Welbes,**

*Acting Deputy Administrator.*

[FR Doc. E9-3208 Filed 2-13-09; 8:45 am]

**BILLING CODE 4910-57-P**

**DEPARTMENT OF TRANSPORTATION****Federal Transit Administration****49 CFR Part 612**

[Docket No. FTA-2008-0005]

RIN 2132-AA96

**Contractor Performance Incentives for the Capital Investment Program**

**AGENCY:** Federal Transit Administration (FTA), DOT.