

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1308

[DEA Number 162P]

**Schedules of Controlled Substances:
Proposed Removal of Fenfluramine
From the Controlled Substances Act****AGENCY:** Drug Enforcement Administration (DEA), Justice.**ACTION:** Notice of proposed rulemaking.

SUMMARY: This proposed rule is issued by the Acting Deputy Administrator of the DEA to remove the anorectic drug, fenfluramine, including its salts, isomers and salts of isomers from control under the Controlled Substances Act (CSA). This proposed action is based upon a finding by the Acting Deputy Administrator of the DEA that the data collected and reviewed to date are insufficient to establish that fenfluramine has sufficient potential for abuse and dependence to justify its continued control in any schedule at this time. This rule, if finalized, would remove all regulatory controls and criminal sanctions of the CSA from activities involving fenfluramine.

DATES: Comments, objections, and requests for a hearing must be received on or before July 7, 1997.

ADDRESSES: Comments, objections and requests for a hearing should be submitted in quintuplicate to the Acting Deputy Administrator, Drug Enforcement Administration, Washington, DC 20537, Attn: DEA Federal Register Representative/CCR.

FOR FURTHER INFORMATION CONTACT: Frank Sapienza, Chief, Drug and Chemical Evaluation Section, Drug Enforcement Administration, Washington, D.C. 20537, (202) 307-7183.

SUPPLEMENTARY INFORMATION: Fenfluramine is an anorectic indicated for the management of exogenous obesity that was first approved for marketing in the United States under the trade name of Pondimin in 1973. Fenfluramine, its salts, isomers and salts of isomers, were placed into Schedule IV of the CSA effective on June 15, 1973 because fenfluramine was determined to be chemically and pharmacologically similar to amphetamine and other anorectic drugs controlled under the CSA. This action was based on a recommendation by the Acting Assistant Secretary for Health, Interneuron Pharmaceuticals, Inc., the manufacturer of a new fenfluramine product (Redux, approved by the Food

and Drug Administration for marketing in the United States in April 1996) petitioned the DEA on March 18, 1991 to decontrol fenfluramine, citing a lack of actual or potential for abuse. The DEA Administrator, after gathering available data and conducting an initial review of that data, requested a scientific and medical evaluation and scheduling recommendation from the Assistant Secretary for Health, Department of Health and Human Services (DHHS) by letter dated December 2, 1991 in accordance with 21 U.S.C. 811(b). DHHS provided its medical and scientific evaluation and scheduling recommendation on fenfluramine to the DEA by letter dated June 3, 1996. The Assistant Secretary for Health concluded that fenfluramine does not warrant control under the CSA and recommended to the DEA that fenfluramine be decontrolled. The Assistant Secretary for Health provided a written scientific and medical evaluation which formed the basis for the recommendation.

The DHHS evaluation considered reports in the scientific and medical literature (1968–1995), adverse reaction reports (1973–1995), data from the Drug Abuse Warning Network (DAWN) (1985–1993), the System to Retrieve Information from Drug Evidence (STRIDE) (1973–1991), marketing data (1990–1993) and other sources of information. Data from the scientific and medical literature demonstrate that fenfluramine is not an amphetamine-like stimulant. Fenfluramine does not maintain self-administration as evidenced by studies in several species (rhesus monkeys, baboons, dogs or rodents). In drug discrimination studies in humans and laboratory animals, the effects of fenfluramine differed from those of amphetamine and cocaine. In human studies, the subjective effects of fenfluramine were found to differ from those of other amphetamine-like anorectics. Fenfluramine however, at high doses, displays complete generalization to MDMA in rodents. Subjective evaluation studies of high doses of fenfluramine in humans shows that in some cases it produces euphoria alternating with dysphoria. The DHHS reported that although high doses of fenfluramine may result in LSD-like responses, these have been characterized by dysphoric. Clinical data does not show that the use of fenfluramine or dexfenfluramine at high doses leads to dependence to the same extent as other substances in Schedules IV or V. The DHHS found the risks to the public health resulting from the abuse of fenfluramine to be similar to

the abuse or misuse of any other agent that is taken outside of appropriate medical direction. However, the DHHS did cite neurotoxic consequences and primary pulmonary hypertension in humans as possible safety risks associated with fenfluramine use. The DHHS review also indicates that based upon over 20 years of marketing of fenfluramine in the United States and elsewhere, abuse of fenfluramine has not been demonstrated to result in either physical or psychic dependence that would lead to craving of the desire to re-initiate the drug upon discontinuation of use. The document indicates that reports of actual abuse, diversion and withdrawal syndrome have been collected but are considered isolated. The significance of these reports, relative to the production of dependence to the same extent as other substances in Schedules IV or V, has not been established.

The DHHS, in its evaluation, however, noted that there had been limited sales and prescribing of fenfluramine from 1973 to 1992, thus data on abuse, diversion and trafficking of fenfluramine would be expected to be minimal. DHHS reported a recent dramatic increase in usage of fenfluramine, particularly in combination with phentermine, a Schedule IV controlled substance. DHHS noted that this could be reason for concern because the long-term use could significantly impact the public health.

While the recommendations of DHHS are binding on DEA regarding scientific and medical matters, the recommendation to decontrol fenfluramine is not binding on the DEA because fenfluramine is currently controlled under the CSA. The DEA must consider the DHHS recommendation and all other relevant data prior to making a determination as to whether substantial evidence of potential for abuse exists so as to warrant continued control of fenfluramine under the CSA. Thus, the DEA examined the DHHS recommendation, supplemented by more recent abuse, diversion, and trafficking data in light of the following factors determinative of control or removal of a drug or other substance from the schedules [21 U.S.C. 811(c)]:

- (1) Its actual or relative potential for abuse.
- (2) Scientific evidence of its pharmacological effect, if known.
- (3) The state of current scientific knowledge regarding the drug or other substance.
- (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.

(8) Whether the substance is an immediate precursor of a substance already controlled under the CSA.

In addition to the DHHS data, the DEA review shows that:

(1) DAWN, forensic laboratory data and associated federal investigative files show very little abuse, trafficking and diversion of fenfluramine. A few DEA Field Offices have reported increases in fenfluramine purchases by physicians and pharmacies accompanied by indiscriminate prescribing of fenfluramine, often in combination with phentermine. The U.S. Customs Service has documented seizures of illegally imported fenfluramine tablets into the United States, that were repackaged and shipped to Mexican pharmacies. The significance of these reports in terms of fenfluramine's abuse potential is unknown as of this time. The levels of abuse, trafficking and diversion identified thus far for fenfluramine are less than those of similarly controlled substances.

(2) State authorities including Boards of Pharmacy, Boards of Medical Examiners, Departments of Health, and police crime laboratories were queried and reported little or no documented actual abuse, trafficking and diversion at this time. DEA received input from 36 state agencies and the District of Columbia. The majority of state drug regulatory agencies reported that they had no evidence that fenfluramine is trafficked or abused. There were a few cases reported where patients had obtained fenfluramine through unauthorized prescription refills, fraudulent prescriptions, doctor shopping, illegal sales, mail order schemes and thefts. However, these reports generally include phentermine and their association with fenfluramine abuse has not been established. Very few state police crime laboratories reported cases involving fenfluramine.

(3) Fenfluramine has been marketed in the U.S. since 1973, with little therapeutic use until recently when the combination of phentermine and fenfluramine emerged. The number of prescriptions for fenfluramine has increased dramatically since 1992 and has more than doubled each year since 1994. Total prescriptions dispensed in the United States in 1992 for fenfluramine were less than 100,000. In 1996, total prescriptions dispensed in the United States totalled over 5.1

million, an increase of 6100 percent in four years.

The Acting Deputy Administrator of the DEA, based on the DHHS evaluation and the DEA review, has concluded that there is insufficient data available at this time to establish that fenfluramine has a potential for abuse which warrants control under the CSA. Nevertheless, it is unclear whether the low levels of abuse, trafficking and diversion are due to the fact that only recently fenfluramine became available in significant quantities or if the low levels of data are an indication that fenfluramine lacks abuse potential. Therefore, in light of the increasing availability and use of fenfluramine, particularly in combination with phentermine, and possible public health and safety risks including neurotoxicity, primary pulmonary hypertension and reports that fenfluramine may have pharmacological similarity to some hallucinogenic substances, the DEA will carefully monitor the abuse, trafficking and diversion indicators regarding this substance. If this data indicates the need for a reexamination of the control status of fenfluramine, the DEA will re-initiate the evaluation process as set forth in the CSA [21 U.S.C. 811(b)].

Relying on the scientific and medical evaluation and the recommendation of the Assistant Secretary of Health received in accordance with 21 U.S.C. 811(b), and the independent review of the DEA, the Acting Deputy Administrator of the DEA, pursuant to Section 201(b) of the Act [21 U.S.C. 811(b)], has determined that these facts and all other relevant data constitute substantial evidence that fenfluramine should be removed entirely from the schedules.

Interested persons are invited to submit their comments, objections or requests for a hearing, in writing, 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 Acting Deputy Administrator, Drug Enforcement Administration, Washington, D.C. 20537. Attention: DEA Federal Register Representative. In the event that comments, objections or requests for a hearing raise one or more issues which the Acting Deputy Administrator finds warrants a hearing, the Acting 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.

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 (E.O.) 12866, Section 3(d)(1).

The Acting 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-business entities. Fenfluramine is available in drug products for the treatment of obesity, some of which have been marketed in the United States for a number of years. This proposed rule, if finalized, will allow persons to handle fenfluramine without being subject to the regulatory controls of the CSA. Fenfluramine will continue to be a prescription drug.

This rule will 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 their various levels of government. States may choose to decontrol fenfluramine or continue to control it under their respective CSA. Therefore, in accordance with E.O. 12612, it is determined that this rule, if finalized, does not have sufficient federalism implications to warrant the preparation of a Federalism Assessment.

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 the DEA by the Department of Justice regulations (28 CFR 0.100) and redelegate to the Acting Deputy Administrator pursuant to 28 CFR 0.104, the Acting Deputy Administrator hereby proposes that 21 CFR part 1308 be amended as follows:

PART 1308—[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.

§ 1308.14 [Amended]

2. Section 1308.14 is proposed to be amended by removing the existing paragraph (d) and by redesignating the existing paragraphs (e) and (f) as (d) and (e), respectively.

Dated: April 29, 1997.

James S. Milford,

Acting Deputy Administrator.

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DEPARTMENT OF THE TREASURY

Bureau of Alcohol, Tobacco and Firearms

27 CFR Part 9

[Notice No. 851 (97-105)]

RIN: 1512-AA07

Davis Mountains Viticultural Area

AGENCY: Bureau of Alcohol, Tobacco and Firearms (ATF), Department of the Treasury.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Bureau of Alcohol, Tobacco and Firearms (ATF) is considering the establishment of a viticultural area located in Jeff Davis County, Texas, to be known as "Davis Mountains." This proposal is the result of a petition filed by Maymie Nelda Weisbach of Blue Mountain Vineyard, Inc. ATF believes that the establishment of viticultural areas and the subsequent use of viticultural area names as appellations of origin in wine labeling and advertising allows wineries to designate the specific areas where the grapes used to make the wine were grown and enables consumers to better identify the wines they purchase.

DATES: Written comments must be received by July 7, 1997.

ADDRESSES: Send written comments to: Chief, Wine, Beer and Spirits Regulations Branch, Bureau of Alcohol, Tobacco and Firearms, P.O. Box 50221, Washington, DC 20091-0221, Attn: Notice No. 851. Copies of written comments received in response to this notice of proposed rulemaking will be available for public inspection during normal business hours at: ATF Reference Library, Document Services Branch, Room 6300, 650 Massachusetts Avenue, NW, Washington, DC 20226.

FOR FURTHER INFORMATION CONTACT: Marjorie D. Ruhf, Wine, Beer and Spirits Regulations Branch, Bureau of Alcohol, Tobacco and Firearms, 650 Massachusetts Avenue, NW., Washington, DC 20226 (202-927-8230).

SUPPLEMENTARY INFORMATION:

Background

On August 23, 1978, ATF published Treasury Decision ATF-53 (43 FR 37672, 54624) revising regulations in 27

CFR part 4. These regulations allow the establishment of definite American viticultural areas. The regulations also allow the name of an approved viticultural area to be used as an appellation of origin in the labeling and advertising of wine.

On October 2, 1979, ATF published Treasury Decision ATF-60 (44 FR 56692) which added a new part 9 to 27 CFR, providing for the listing of approved American viticultural areas. Section 4.25a(e)(1), title 27, CFR, defines an American viticultural area as a delimited grape-growing region distinguishable by geographical features, the boundaries of which have been delineated in subpart C of part 9. Section 4.25a(e)(2) outlines the procedure for proposing an American viticultural area. Any interested person may petition ATF to establish a grape-growing region as a viticultural area. The petition should include:

(a) Evidence that the name of the proposed viticultural area is locally and/or nationally known as referring to the area specified in the petition;

(b) Historical or current evidence that the boundaries of the viticultural area are as specified in the petition;

(c) Evidence relating to the geographical features (climate, soil, elevation, physical features, etc.) which distinguish the viticultural features of the proposed area from surrounding areas;

(d) A description of the specific boundaries of the viticultural area, based on features which can be found on United States Geological Survey (U.S.G.S.) maps of the largest applicable scale; and

(e) A copy of the appropriate U.S.G.S. map(s) with the boundaries prominently marked.

Petition

ATF has received a petition from Maymie Nelda Weisbach, of Blue Mountain Vineyard, Inc., proposing to establish a viticultural area in Jeff Davis County, Texas, to be known as "Texas Davis Mountains." The proposed viticultural area is located in the Trans-Pecos region of west Texas. The entire area contains approximately 270,000 acres, of which approximately 40 acres are planted to vineyards. Blue Mountain Vineyard is the only commercial grower currently active within the proposed viticultural area.

Evidence of Name

The petitioner provided evidence that the name "Davis Mountains" is locally known as referring to the area specified in the petition, and proposed that the area be designated as "Texas Davis

Mountains" to aid in national recognition of the area. She noted that, outside of the State of Texas, the name Davis Mountains may not be well known. Evidence supporting the use of the name "Davis Mountains" includes:

(a) One of the U.S.G.S. maps used to show the boundaries of the proposed area (Mount Livermore, Texas—Chihuahua) uses the name "Davis Mountains" to identify the northern portion of the proposed area. There is a park named "Davis Mountain State Park" in the southeastern portion of the proposed area. The map shows no conflicting designation for the remainder of the proposed area.

(b) The petitioner provided an excerpt from the 1952 edition of *The Handbook of Texas*, published by the Texas State Historical Association, which describes the Davis Mountains. The location and other features described in this entry are consistent with the petition.

(c) The petitioner also provided an excerpt from the 1968 edition of *Texas Today*, a book in the Harlow State Geography Series, from the Harlow Publishing Corporation. In it, the Davis Mountains are described as the most extensive and among the highest of the Texas mountain groups.

(d) Finally, the petitioner provided copies of two highway maps, the Champion Map of Texas, and the Exxon Travel Club Map of the United States, both of which identify the Davis Mountains by name.

ATF reviewed available resources and found no references to any other "Davis Mountains." There is national recognition of the name "Davis Mountains" as an area in Texas, known for the McDonald Observatory, which is located there, and as a tourist destination for its history, scenery and wildlife. For purposes of this notice, the name "Davis Mountains" will be used as the name for the proposed area. Comments on the need for further clarification of this name are solicited in the Public Participation section of this notice.

Evidence of Boundaries

The petitioner has defined the proposed area primarily by highways which, she states, parallel geographic features which define the area. In support of this approach, the petitioner provided a copy of "Texas," the *Houston Chronicle* Magazine, for June 2, 1996. The cover story was "High mountain vistas, driving the 73-mile loop around the Davis Mountains." In a map associated with the article, the routes used for the driving tour are the same as those selected by the petitioner, except the northern boundary. The