Regulatory Flexibility and Executive Order 12291

The Deputy Assistant Administrator hereby certifies that this proposal will have no significant impact upon small businesses or other entities whose interests must be considered under the Regulatory Flexibility Act, 5 U.S.C. 601, et seq. A small percentage of registered practitioners will be dispensing Food and Drug Administration approved drug products which consist of dronabinol in sesame oil and encapsulated in soft gelatin capsules due to the limited medical indication for such products.

Pursuant to section 3(c) 3 and 3(e)(B) of Executive Order 12291 (46 FR 13193), this proposed action has been submitted for review by the Office of Management and Budget, and approval of that Office has been requested pursuant to the provisions of the Paperwork Reduction Act of 1980, 44 U.S.C. 3501, et seq.

Dated: October 1, 1985.

Gene R. Haislip,

Deputy Assistant Administrator, Office of Diversion Control, Drug Enforcement Administration.

[FR Doc. 85-24908 Filed 10-17-85; 8:45 am]

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21 CFR Part 1308

Schedules of Controlled Substances; Rescheduling of Synthetic Dronabinol in Sesame Oil and Encapsulated in Soft Gelatin Capsules From Schedule I to Schedule II

AGENCY: Drug Enforcement Administration, Justice.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Administrator of the Drug Enforcement Administration (DEA) issues this notice of proposed rulemaking to remove drug products which consist of dronabinol in sesame oil and encapsulated in soft gelatin capsules from Schedule I and place them into Schedule II of the Controlled Substances Act (CSA), 21 U.S.C. 801, et seq. Dronabinol in the synthetic equivalent of the isomer of delta-9-tetrahydrocannebinol which is the principal pyschoactive substance in *Cannabis sativa L.*, marijuana. This action follows the Administrator's review of the CSA, the Controlled Substances Import and Export Act, the Convention on Psychotropic Substances 1971, the Assistant Secretary for Health's recommendation and the Food and Drug Administration's (FDA) approval for marketing of Marinol Capsules. This rule will require that the manufacture, distribution, dispensing, security, registration, record keeping, reporting, inventory, exportation and importation of a drug product which consists of dronabinol in sesame oil and encapsulated in soft gelatin capsules be subject to controls for Schedule II substances. Additional controls necessitated by the listing of delta-9-tetrahydrocannabinol in Schedule I of the Convention on Psychotropic Substances 1971 are addressed in a separate notice published elsewhere in this issue of the **Federal Register**. The proposed rule is intended to affect the CSA schedule of pharmaceutical products approved for marketing by the FDA, and is not intended to affect the Schedule I status of any other substance, mixture or preparation which is currently included in 21 CFR 1308.11(d)(21), Tetrahydrocannabinols.

DATE: Comments and objections must be received on or before November 18, 1985.

ADDRESS: Comments and objections should be submitted in quintuplicate to the Administrator, Drug Enforcement Administration, 1405 I Street, NW., Washington, DC 20537, Attention: DEA Federal Register Representative.

FOR FURTHER INFORMATION CONTACT: Howard McClain, Jr., Chief, Drug Control Section, Drug Enforcement Administration, Washington, DC 20537, Telephone: (202) 633-1366.

SUPPLEMENTARY INFORMATION:

List of Subjects in 21 CFR Part 1308

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

On May 31, 1985, the Food and Drug Administration (FDA) approved the new drug application for the product, Marinol Capsules, which was submitted by Unimed Incorporated. The product contains specified quantities of dronabinol in sesame oil and encapsulated in round soft gelatin capsules. Dronabinol is the U.S. Adopted Name (USAN) for the substance (6a*R-trans*)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6*H*-dibenzo[*b,d*]pyran-1-ol or (-)-delta-9-(trans)-tetrahydroncannabinol, the principal psychoactive substance in *Cannabis sativa L.*, marijuana. The drug product is approved for the treatment of the nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional anitemetic treatments.

Dronabinol is an isomer of D^1 cis or trans tetrahydrocannabinol. Accordingly, dronabinol and any material, compound, mixture or preparation which contains any quantity of dronabinol are Schedule I substances [see 21 CFR 1308.11(d)(21)]. Thus, Marinol Capsules, the FDA approved drug product, cannot be legally marketed until it is rescheduled.

By letter of August 16, 1982, the Assistant Secretary for Health notified the then Acting Administrator of his scheduling recommendations relative to tetrahydrocannabinol (THC) pursuant to 21 U.S.C. 811(b). The Assistant Secretary recommended that THC remain in Schedule I of the CSA but that it be rescheduled to Schedule II if a new drug application was approved by FDA. (The Assistant Secretary's submission described THC as (-)-delta-9-(trans)-tetrahydrocannabinol, which has since been named dronabinol and is contained in Marinol Capsules.) These recommendations were based on the FDA's consideration of the eight factors and scheduling criterial listed in 21 U.S.C. 811(c) and 812(b).

Dela-9-tetrahydrocannabinol, its salts, stereochemical variants and salts of the stereochemnical variants are listed in Schedule I of the Convention on Psychotropic Substances 1971. The United States is a party to that international convention pursuant to the Psychotropic Substances Act of 1978 (Pub. L. 95-633, November 10, 1978). The Attorney General is responsible for carrying out certain of the United States obligations under this convention.

Article 7 of the convention reads as follows:

Special Provisions Regarding Substances in Schedule I

In respect to substances in Schedule I, the Parties shall:

(a) Prohibit all use except for scientific and very limited medical purposes by duly authorized persons, in medical or scientific establishments which are directly under the control of their Governments or specifically approved by them;

(b) Require that manufacture, trade, distribution and possession be under special license or prior authorization;

(c) Provide for close supervision of the activities and acts mentioned in paragraphs (a) and (b);

(d) Restrict the amount supplied to a duly authorized person to the quantity required for his authorized purpose;

(e) Require that persons performing medical or scientific functions keep records concerning the acquisition of the substances and the details of their use, such record to be preserved for a least two years after the last use recorded therein; and

(f) Prohibit export and import except when both the exporter and importer are the competent authorities or agencies of the exporting and importing country or region, respectively, or other persons or enterprises which are specifically authorized by the competent authorites of their country or region for the purpose. The requirements of

paragraph 1 of article 12 for export and import authorizations for substances in Schedule II shall also apply to substances in Schedule I.

The CSA requires compliance with the U.S. obligations under the international drug control treaties and mandates effective controls against the diversion of controlled substances into other than legitimate medical and scientific channels while enabling medical practitioners and their patients to obtain medically approved and necessary controlled substances. The Administrator has determined that domestic and international obligations will be satisfied by the transfer of the FDA approved product from Schedule I to Schedule II of the CSA and by the retention of all other forms of THC in Schedule I. In addition to the requirements associated with Schedule II substances, the Administrator has determined that the obligations associated with article 7 of the convention require strict adherence to the FDA approved indication for use of the product and limitation of export of the product to that between competent authorities or agencies of countries or regions. To insure compliance with these obligations, changes in the protocol requirements for researchers and prescription requirements for practitioners are proposed in a Notice published elsewhere in this issue of the Federal Register. Further, the Administration has determined that the description of the Schedule II substance must be such that identification of the material will not create an undue burden for those who are responsible for enforcing the CSA and the laws of the several states.

Based upon the investigations and review of the Drug Enforcement Administration with attention to the U.S. obligations under the Convention on Psychotropic Substances 1971 and relying on the sceintific and medical evaluation and recommendation of the Assistant Secretary for Health of the Department of Health and Human Services in accordance with 21 U.S.C. 811(b), and the Food and Drug Administration approval of a new drug application for Marinol Capsules, the Administrator of the Drug Enforcement Administration, pursuant to the provisions of 21 U.S.C. 811(a), finds that:

1. Dronabinol (synthetic) in seasame oil and encapsulated in soft gelatin capsules in a U.S. Food and Drug Administration approved drug product has a high potential for abuse;

2. Dronabinol (synthetic) in seseme oil and encapsulated in soft gelatin capsules in a U.S. Food and Drug Administration approved drug product has a currently accepted medical use in treatment in the United States or a currently accepted medical use with severe restrictions; and,

3. Dronabinol (synthetic) in seasame oil and encapsulated in soft gelatin capsules in a U.S. Food and Drug Administration approved drug product may lead to severe psychological or physical dependence.

Pursuant to the authority vested in the Attorney General by section 201(a) of the CSA [21 U.S.C. 811(a)], as redelegated to the Administrator of the Drug Enforcement Administration by 28 CFR 0.100, and for the reasons set forth above, the Administrator hereby proposes to amend 21 CFR 1308.11 and 1308.12 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).

2. 21 CFR 1308.11(d)(21) is revised to read as follows:

§ 1308.11 Sechedule I.

* * * * *

(d) *Hallucinogenic substances.* * * *

(21) Tetrahydrocannabinols.....7370

Synthetic equivalents of the substances contained in the plant, or in the resinous extractives of *Cannabis* sp. and/or synthetic substances, derivatives, and their isomers with similar chemical structure and pharmacological activity such as the following:

Δ^1 cis or trans tetrahydrocannabinol, and their optical isomers, excluding dronabinol in sesame oil and encapsulated in a soft gelatin capsule in a drug product approved by the U.S. Food and Drug Administration,

Δ^6 cis or trans tetrahydrocannabinol, and their optical isomers,

$\Delta^{3,4}$ cis or trans tetrahydrocannabinol, and its optical isomers. (Since nomenclature of these substances is not internationally standardized, compounds of these structures, regardless of numerical designation of atomic positions are covered.)

* * * * *

3. 21 CFR 1308.12 is amended by redesignating the existing paragraph (f) as paragraph (g) and by adding a new paragraph (f), reading as follows:

§ 1308.12 Schedule II.

* * * * *

(f) *Hallucinogenic substances.*

(1) Dronabinol (synthetic) in sesame oil and encapsulated in a soft gelatin capsule in a U.S. Food and Drug Administration approved drug product.....7369

[Some other names for dronabinol: (6a*R*-*trans*)-6a,7,8,10a-tetrahydro-6,6,9-trimethyl-3-pentyl-6*H*-dibenzo[*b*,*d*]pyran-1-ol, or (-)-delta-9-(trans)-tetrahydrocannabinol]

* * * * *

All interested persons are invited to submit their comments or objections in writing regarding this proposal. If a person believes that one or more issues raised warrant a hearing, that person should so state and summarize the reasons for this belief. Comments and objections should be submitted in quintuplicate to the Administrator, Drug Enforcement Administration, 1405 I Street, NW., Washington, DC 20537, Attention: DEA Federal Register Representative.

In the event that comments or objections to this proposal raise one or more issues which warrant a hearing, the Administrator will publish in the Federal Register an order for a public hearing which will summarize the issues to be heard and set the time for the hearing that will not be less than 30 days after the date of the order.

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Pursuant to 5 U.S.C. 605(b), the Administrator certifies that the rescheduling of formulations containing dronabinol, as proposed herein, will not have a significant impact upon small businesses or other entities whose interests must be considered under the Regulatory Flexibility Act (Pub. L. 96-345, September 19, 1980). The proposed action will allow the marketing of a drug product which was recently approved by the FDA.

In accordance with the provisions of 21 U.S.C. 811(a), this proposal to reschedule certain drug products which contain synthetic dronabinol from Schedule I to Schedule II 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 have been exempted from the consultation requirements of Executive Order 12291 (46 FR 13193).

Dated: October 11, 1985.

John C. Lawn,

Administrator, Drug Enforcement Administration.

[FR Doc. 85-24907 Filed 10-17-85; 8:45 am]

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