

# Proposed Rules

This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rulemaking prior to the adoption of the final rules.

## DEPARTMENT OF JUSTICE

Bureau of Narcotics and Dangerous Drugs

[ 21 CFR Part 308 ]

### SCHEDULES OF CONTROLLED SUBSTANCES

#### Proposed Placement of Benzphetamine in Schedule III

On February 15, 1973, the Acting Assistant Secretary for Health, on behalf of the Secretary of Health, Education, and Welfare, sent the following letter to the Director of the Bureau of Narcotics and Dangerous Drugs:

DEPARTMENT OF HEALTH, EDUCATION,  
AND WELFARE

OFFICE OF THE SECRETARY

Washington, D.C. 20201

FEBRUARY 15, 1973.

JOHN E. INGERSOLL,  
Director, Bureau of Narcotics and Dangerous  
Drugs, Department of Justice, 1405 I  
Street NW., Washington, D.C. 20537

DEAR MR. INGERSOLL: The Food and Drug Administration has recently completed a review of all drugs currently marketed or proposed for marketing in the United States for the treatment of obesity. The marketed drugs include three substances already controlled under schedule II of the Controlled Substances Act, amphetamine, methamphetamine, and phenmetrazine. The review also included drugs currently not controlled under any schedule, the marketed drugs, diethylpropion, benzphetamine, phendimetrazine, phentermine, and chlorphentermine, and the investigational substances, clortermine, mazindol, and fenfuramine. New drug applications have been submitted to the Food and Drug Administration for the latter three drugs, and approval is pending.

Review of data reveals that these drugs produce approximately the same degree of therapeutic effects in man as currently scheduled anorectics, as adjuncts in weight reduction in the obese. The review indicated that the drugs are also comparable in other ways to scheduled anorectics:

a. They are all closely related chemically, with the exception of mazindol.

b. Their pharmacological profiles are closely similar, except for certain aspects of the profile of fenfuramine.

c. Documentation of actual abuse or production of dependence in humans is irregular, but does exist for certain of the unscheduled anorectics. The skimpy documentation of abuse of these drugs appears due to the fortuitous nature of reports as currently obtained and to the past easy availability of cheaper and more potent stimulants, rather than to intrinsic lack of abuse potential.

d. We note the conclusions and recommendations of the WHO Expert Committee on Drug Dependence that these drugs either be subject to control or by analogy are similar to drugs recommended for control.

e. Certain specialized testing of fenfuramine suggests that the abuse potential of fenfuramine is of a lower order of magnitude

than that of the other drugs under consideration.

We, therefore, conclude that all the above-named drugs possess abuse potential and potential for producing drug dependence, and are so informing you as required under the provisions of section 201(f) of the Controlled Substances Act. As provided for by section 201(a), we further request that the Attorney General issue rules adding the above drugs to the schedules of the Controlled Substances Act, and recommend that the schedule for all drugs but fenfuramine be schedule III, fenfuramine appearing more appropriately controlled under the provisions of schedule IV.

We attach review material assembled by reviewing pharmacologists within the Food and Drug Administration for its possible utility to you, and as a basis for further discussion after your scientists have reviewed our recommendations and request.

Sincerely,

RICHARD L. SEGEL,  
Acting Assistant Secretary  
for Health.

Upon receipt of this letter, the Bureau undertook a review of the following: (1) Materials submitted to BNDD by the Department of Health, Education, and Welfare with the letter of February 15, 1973; (2) materials submitted to the Food and Drug Administration in connection with new drug applications on these drugs; (3) published scientific and medical literature from the United States and other nations regarding these drugs; (4) selected investigatory files compiled for law enforcement purposes by the Bureau and another law enforcement agency; and (5) the legislative history of the Controlled Substances Act.

The results of this review can be summarized as follows:

(1) Benzphetamine is chemically similar to and related to the other anorectic drugs being proposed for control, and to amphetamine, methamphetamine, and phenmetrazine, substances currently listed in schedule II.

(2) Benzphetamine has a pharmacological profile which is similar to the other anorectic drugs being proposed for control and to amphetamine, methamphetamine, and phenmetrazine. This general similarity suggests that all of these drugs may be reasonably substituted for each other for therapeutic or abuse purposes.

(3) Benzphetamine is covered by a new drug application approved by the Food and Drug Administration for use in treatment of obesity.

(4) Products containing benzphetamine, chlorphentermine, diethylpropion, phendimetrazine, or phentermine have been marketed in the United States for several years. In the last 6 months, certain of these products have been reported as the subject of thefts, diversion,

illicit sales, and abuse. Quantitatively, this data does not suggest a widespread problem at the present time; qualitatively, the data indicates a trend to substitute these products for amphetamine and methamphetamine preparations in abuse circles. This reinforces the belief that abuse of the pharmacologically similar drugs will increase as the amphetamines and methamphetamine become less and less available.

(5) The legislative history of the Controlled Substances Act makes clear that the Bureau is to schedule drugs based upon their potential for abuse, and "should not be required to wait until a number of lives have been destroyed or substantial problems have arisen before designating a drug as subject to controls." (Comprehensive Drug Abuse Prevention and Control Act of 1970, House Report 91-1444 (part 1), p. 35, Sept. 10, 1970) Discussing factors used to measure potential for abuse, the report quotes from the regulations issued under the Drug Abuse Control Amendments of 1965 (id. at p. 34):

"The Director may determine that a substance has a potential for abuse because of its depressant or stimulant effect on the central nervous system or its hallucinogenic effect if:

"(1) There is evidence that individuals are taking the drug or drugs containing such a substance in amounts sufficient to create a hazard to their health or to the safety of other individuals or of the community; or

"(2) There is significant diversion of the drug or drugs containing such a substance from legitimate drug channels; or

"(3) Individuals are taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice from a practitioner licensed by law to administer such drugs in the course of his professional practice."

The House Report goes on to say (id. at p. 35):

"In speaking of 'substantial' potential [for abuse] the term 'substantial' means more than a mere scintilla of isolated abuse, but less than a preponderance. Therefore, documentation that, say, several hundred thousand dosage units of a drug have been diverted would be 'substantial' evidence of abuse despite the fact that tens of millions of dosage units of that drug are legitimately used in the same time period."

The Director has concluded from this review of the current situation that control of all anorectic drugs is desirable at this time to insure that they will not become widely abused. This scheduling will fulfill the congressional mandate to act before substantial problems have arisen.

Based upon the investigations and review of the Bureau of Narcotics and Dangerous Drugs and upon the scientific and medical evaluation and recommen-

dation of the Secretary of Health, Education, and Welfare, received pursuant to sections 201(a) and (b) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 811(a), (b)), the Director of the Bureau of Narcotics and Dangerous Drugs finds that:

1. Based on information now available, benzphetamine has a potential for abuse less than the drugs or other substances currently listed in schedule II. Although chemically and pharmacologically this drug is closely related to the other anorectic drugs being proposed for control and to the stimulants now listed in schedule II, present data regarding excessive usage, diversion, illicit sales, and abuse of benzphetamine is not substantial enough to warrant a finding that it has a potential for abuse equal to the stimulants in schedule II.

2. Benzphetamine has a currently accepted medical use in treatment in the United States.

3. Abuse of benzphetamine may lead to high psychological dependence.

Therefore, under the authority vested in the Attorney General by section 201(a) of the Comprehensive Drug Abuse Prevention and Control Act of 1970 (21 U.S.C. 811(a)), and delegated to the Director of the Bureau of Narcotics and Dangerous Drugs by § 0.100 of title 28 of the Code of Federal Regulations, the Director proposes that § 308.13 of title 21 of the Code of Federal Regulations be amended to read:

§ 308.13 Schedule III.

(b) *Stimulants*.—Unless specifically excepted or unless listed in another schedule, any material, compound, mixture, or preparation which contains any quantity of the following substances having a stimulant effect on the central nervous system, including its salts, isomers (whether optical, position, or geometric), and salts of such isomers, whenever the existence of such salts, isomers, and salts of isomers is possible within the specific chemical designation:

- |   |      |
|---|------|
| (1) Those compounds, mixtures, or preparations in dosage unit form containing any stimulant substances listed in schedule II which compounds, mixtures, or preparations were listed on August 25, 1971, as excepted compounds under § 308.32, and any other drug of the quantitative composition shown in that list for those drugs or which is the same except that it contains a lesser quantity of controlled substances | 1405 |
| (2) Benzphetamine   | 1230 |

Conferences have been held between the Bureau and Upjohn Co., the only manufacturer of benzphetamine in bulk or dosage form in the United States. The Upjohn Co. has fully cooperated with the Bureau and has consented to the placement of benzphetamine in schedule III to insure that it does not become subject to abuse in the future.

All other interested persons are invited to submit their comments or objections in writing regarding this pro-

posal. These comments or objections should state with particularity the issues concerning which the person desires to be heard. Comments and objections should be submitted in quintuplicate to the Hearing Clerk, Office of Chief Counsel, Bureau of Narcotics and Dangerous Drugs, Department of Justice, room 611, 1405 Eye Street NW., Washington, D.C. 20537, and must be received no later than June 7, 1973.

In the event that an interested party submits objections to this proposal which present reasonable grounds for this rule not to be finalized and requests a hearing in accordance with 21 CFR 308.45, the party will be notified by registered mail that a hearing on these objections will be held at 10 a.m. on June 11, 1973, in room 1210, 1405 Eye Street NW., Washington, D.C. 20537. If objections submitted do not present such reasonable grounds, the party will be so advised by registered mail.

If no objections presenting reasonable grounds for a hearing on the proposal are received within the time limitations, and all interested parties waive or are deemed to waive their opportunity for the hearing or to participate in the hearing the Director may cancel the hearing and after giving consideration to written comments, issue his final order pursuant to 21 CFR § 308.48 without a hearing.

Dated May 1, 1973.

JOHN E. INGERSOLL,  
Director, Bureau of Narcotics  
and Dangerous Drugs.

[FR Doc.73-9066 Filed 5-8-73;8:45 am]

#### [ 21 CFR Part 308 ]

### SCHEDULES OF CONTROLLED SUBSTANCES

#### Proposed Placement of Chlorphentermine in Schedule III

On February 15, 1973, the Acting Assistant Secretary for Health, on behalf of the Secretary of Health, Education, and Welfare, sent the following letter to the Director of the Bureau of Narcotics and Dangerous Drugs:

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

OFFICE OF THE SECRETARY  
Washington, D.C. 20201

FEBRUARY 15, 1973.

JOHN E. INGERSOLL,  
Director, Bureau of Narcotics and Dangerous Drugs, Department of Justice, 1405 Eye Street NW., Washington, D.C. 20537

DEAR MR. INGERSOLL: The Food and Drug Administration has recently completed a review of all drugs currently marketed or proposed for marketing in the United States for the treatment of obesity. The marketed drugs include three substances already controlled under Schedule II of the Controlled Substances Act, amphetamine, methamphetamine, and phenmetrazine. The review also included drugs currently not controlled under any schedule, the marketed drugs, diethylpropion, benzphetamine, phendimetrazine, phentermine, and chlorphentermine, and the investigational substances, clortermine, mazindol, and fenfluramine. New drug applica-

tions have been submitted to the Food and Drug Administration for the latter three drugs, and approval is pending.

Review of data reveals that these drugs produce approximately the same degree of therapeutic effects in man as currently scheduled anorectics, as adjuncts in weight reduction in the obese. The review indicated that the drugs are also comparable in other ways to scheduled anorectics:

a. They are all closely related chemically, with the exception of mazindol.

b. Their pharmacological profiles are closely similar, except for certain aspects of the profile of fenfluramine.

c. Documentation of actual abuse or production of dependence in humans is irregular, but does exist for certain of the unscheduled anorectics. The skimpy documentation of abuse of these drugs appears due to the fortuitous nature of reports as currently obtained and to the past easy availability of cheaper and more potent stimulants, rather than to intrinsic lack of abuse potential.

d. We note the conclusions and recommendations of the WHO Expert Committee on Drug Dependence that these drugs either be subject to control or by analogy are similar to drugs recommended for control.

e. Certain specialized testing of fenfluramine suggests that the abuse potential of fenfluramine is of a lower order of magnitude than that of the other drugs under consideration.

We, therefore, conclude that all the above named drugs possess abuse potential and potential for producing drug dependence, and are so informing you as required under the provisions of section 201(f) of the Controlled Substances Act. As provided for by section 201(a), we further request that the Attorney General issue rules adding the above drugs to the schedules of the Controlled Substances Act, and recommend that the schedule for all drugs but fenfluramine be schedule III, fenfluramine appearing more appropriately controlled under the provisions of schedule IV.

We attach review material assembled by reviewing pharmacologists within the Food and Drug Administration for its possible utility to you, and as a basis for further discussion after your scientists have reviewed our recommendations and request.

Sincerely,

RICHARD L. SEGGERL,  
Acting Assistant Secretary  
for Health.

Upon receipt of this letter, the Bureau undertook a review of the following: (1) Materials submitted to BNDD by the Department of Health, Education, and Welfare with the letter of February 15, 1973; (2) materials submitted to the Food and Drug Administration in connection with new drug applications on these drugs; (3) published scientific and medical literature from the United States and other nations regarding these drugs; (4) selected investigatory files compiled for law enforcement purposes by the Bureau and another law enforcement agency; and (5) the legislative history of the Controlled Substances Act.

The results of this review can be summarized as follows:

(1) Chlorphentermine is chemically similar to and related to the other anorectic drugs being proposed for control, and to amphetamine, methamphetamine and phenmetrazine, substances currently listed in schedule II.