CONTAINING ANY STIMULANT SUBSTANCES LISTED IN SCHEDULE II WHICH COMBINE 'POUNDS, MIXTURES, OR PREPARATIONS WERE LISTED ON AUGUST 25, 1971, AS EXCEPTED COMPOUNDS UNDER § 308.48, AND ANY OTHER DRUG OF THE QUANTITATIVE COMPOSITION SHOWN IN THAT LIST FOR WHICH THE DEPARTMENT OF JUSTICE HAS CONSENTED TO THE PLACEMENT OF MAZINDOL 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 PROPOSAL. 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 WRITING TO THE HEARING OFFICER, OFFICE OF CHIEF, BUREAU OF NARCOTICS AND DANGEROUS DRUGS, DEPARTMENT OF JUSTICE, WASHINGTON, D.C. 20537, AND MUST BE RECEIVED NO LATER THAN JUNE 1, 1973.

IN THE EVENT THAT AN INTERESTED PARTY SUBMITS OBJECTIONS TO THIS PROPOSAL WHICH PRESENT REASONABLE GROUNDS FOR THIS RULE NOT TO BE FINALIZED, WE REQUEST A HEARING IN ACCORDANCE WITH 21 CFR § 308.48, 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 REASONABLE GROUNDS, THE PARTY WILL BE ADVISED BY REGISTERED MAIL.

IF NO OBJECTIONS PRESENT REASONABLE GROUNDS FOR A HEARING ON THE PROPOSAL ARE RECEIVED WITHIN THE TIME LIMITATIONS, AND A HEARING IS NOT REQUESTED, THE OPPORTUNITY FOR THE HEARING OR TO PARTICIPATE IN THE HEARING, THE DIRECTOR MAY CANCEL THE HEARING AND, AFTER GIVING CONSIDERATION TO THE 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. 73-3908 Filed 5-8-73; 8:45 am]

SCHEDULES OF CONTROLLED SUBSTANCES

PROPOSED PLACEMENT OF PHENIDMETHANEZINE IN SCHEDULE III

On February 15, 1972, 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, 1972.

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

DEAR MR. INGERSOLL:

The Food and Drug Administration has recently completed a review of all drugs currently listed or proposed for marketing in the United States for the treatment of obesity. The market for these drugs includes 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, phenidmethazine, phentermine, and chlorphentermine, and the investigational substances, clomethiazol, mazindol, and fenfluramine. 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 weight reduction in the obese. The review indicated that the drugs are also comparable in other ways to scheduled agents.

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

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

c. Documentation of actual abuse or production of serious harm to 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 these drugs 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 they are similar to drugs recommended for control.

e. Certain specialized testing of fenfluramine suggests that the abuse potential of fenfluramine and related substances is greater than that of the other drugs under consideration.

We, therefore, conclude that all the abovemenioned drugs possess abuse potential and potential for producing drug dependence, and are so informing you as required under the provisions of section 201(a) 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 value to you, and as a basis for further discussion after your scientists have reviewed our recommendations and request.

Sincerely,

RICHARD L. SEGOL
Acting Assistant Secretary for Health.

Upon receipt of this letter, the Bureau undertook a review of the following:

2. Materials submitted to the Food and Drug Administration in connection with new drug applications on these drugs;
3. Epidemiologic data compiled for law enforcement purposes by other agencies and another law enforcement agency; and
4. The legislative history of the Controlled Substances Act.

The results of this review can be summarized as follows:

1. Phenidmethazine 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. Phenidmethazine has a pharmacologic 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 separately controlled for each other for therapeutic or abuse purposes.

3. Phenidmethazine is covered by a new drug application submitted by the Food and Drug Administration for use in treatment of obesity.

4. Products containing benzphetamine, phentermine, or fenfluramine, or benzphetamine or phenmetrazine, or phenmetrazine, 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 that they 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 control. (Comprehensive Drug Abuse Prevention and Control Act of 1970, H. Rept. 91-1444 (pt. 1), p. 39, 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 be a hazard to their health or to the safety of other individuals of the community; or
PROPOSED RULES

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

"(e) taking the drug or drugs containing such a substance on their own initiative rather than on the basis of medical advice or in pursuance of their professional practice."

The House report goes on to say (id. at p. 357): "In speaking of 'substantial' potential for abuse '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 these drugs 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 these drugs 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 recommendations 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 upon information now available, phendimetrazine has a potential for abuse less than that of 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 phendimetrazine is not sufficient to warrant deleting it from that schedule II primarily because of the relatively recent and limited nature of its marketing.

2. Phendimetrazine has a currently accepted medicinal use in treatment in the United States.

3. Abuse of phendimetrazine 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 II.

(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 stimulating effect on the central nervous system, including its salts, isomers (whether optical, positional, or geometric), and salts of such isomers whenever the use 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 of the substances listed in schedule II which compounds, mixtures, or preparations were listed on August 26, 1971, as excepted compounds under § 303.32, and any other drug of the quantitative composition shown in that list for those drugs or which in the same except that it contains a lower quantity of controlled substances.

2. Phendimetrazine.

Conferences have been held between the Bureau and the Ayerst Laboratories Division of the American Home Products Corp., the largest manufacturer of phendimetrazine in the United States and the only firm with a new drug application for phendimetrazine approved by the Food and Drug Administration. Ayerst laboratories currently cooperate with the Bureau and has consented to the placement of phendimetrazine in schedule II in order to insure that it does not become available in any major form for any other purpose.

All other interested persons are invited to submit their comments or objections in writing regarding this proposal. 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 111, 1405 I 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 the conclusion that there is no basis for a hearing in accordance with 21 CFR 308.45, the party will be notified by registered mail that a hearing on these objections cannot be held at 10 a.m. on June 11, 1973, at 10 a.m. on June 11, 1973. In case the party desires to participate in the hearing, the party should notify the Hearing Clerk in writing on or before June 9, 1973, and file such written objection to this proposal which present reasonable grounds for the conclusion that there is no basis for a hearing, and after being given the opportunity to present evidence in writing, comments, issues his final order pursuant to 21 CFR § 303.43 without a hearing.

Dated May 1, 1973.

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

FEDERAL REGISTER, VOL. 38, NO. 89—WEDNESDAY, MAY 9, 1973

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[21 CFR Part 308] SCHEDULES OF CONTROLLED SUBSTANCES

Proposed Placement of Phentermine in Schedule II

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. 20250


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

Dear Mr. Incecall:

The Food and Drug Administration has recently completed a review of all substances 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 stimulants currently marketed for any schedule other than schedule II of the Act, diet pills, phenmetrazine, and 2, 3-dimethyltryptamine. The review indicates that the drugs are all equally effective chemically, with the exception of fenfluramine. New drug applications have been submitted to the Food and Drug Administration for the latter three drugs, and approval is pending.

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

a. They are all orally administered, chemically, with the exception of fenfluramine.

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

c. Demonstration of actual abuse or potential for abuse that is comparable to or less than that of the currently scheduled anorectics.

The clinical trial of the abuse of these drugs appears due to the similarities noted above in readily available and fenfluramine tablets, rather than to intrinsic lack of abuse potential.

We hereby concur in the 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.

We, therefore, conclude that all the above named drugs possess abuse potential, fulfills the lower order of magnitude that than of the other drugs under consideration.

We, therefore, recommend that the Attorney General, through the Bureau of Narcotics and Dangerous Drugs, take the above drugs to the schedules of the Controlled Substances Act. As provided for by section 201(a), we further request that the Attorney General inform the Congress of any changes in status of these drugs or the schedules of the Controlled Substances Act.