under the Drug Abuse Control Amendments of 1967 (Comprehensive Drug Abuse Prevention and Control Act of 1970, H. Rept. 91–144 (part 1), p. 34, Sept. 10, 1970):

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:

* * * * *

(4) The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

* * * * *

The Director has concluded from this review of the current situation that control of all anorectic drugs is at this time to prevent their becoming widely abused. This scheduling will fulfill the congressional mandate to act before substantial problems have arisen.

Because of the chemical and pharmacological similarities between fenfluramine and the other anorectic drugs being proposed for control, the Bureau is proposing placement of fenfluramine in schedule IV. The Bureau will monitor the manufacture, distribution, and use of fenfluramine in the United States, paying special attention to indicators of diversion (such as shortages in accountability audits of distributors and dispensers, thefts from handlers, and availability on the illicit market) and to other indicators which indicate that fenfluramine is actually being abused (such as excessive prescribing and dispensing, reports of adverse reactions and overdoses, and other medical experiences). The Bureau will also consider, if available, clinical and other research in abusability, dependence-creating, and dependence-sustaining characteristics of fenfluramine. If, after 18 months during which the drug is marketed, experience suggests that fenfluramine has not been subject to significant diversion or abuse, the Director will review the necessity and desirability of maintaining fenfluramine in schedule IV and will request from the Secretary of Health, Education, and Welfare a new scientific and medical evaluation, and his recommendation, as to whether fenfluramine should be so controlled or removed as a controlled substance. Any interested person may petition the Bureau to decontrol fenfluramine at any time.

Based upon the investigations and review of the Bureau of Narcotics and Dangerous Drugs and upon the scientific and medical evaluation and recommendation 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 evaluated up to this time, fenfluramine has a low potential for abuse relative to the drugs or other substances currently listed in schedule III, based on information now available. Although chemically and/or pharmacologically this drug is 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 in other countries is not substantial enough to warrant a finding that fenfluramine has a potential for abuse equal to the stimulants in schedule II or to the seven drugs listed above. In addition, certain tests cited in the letter from the Department of Health, Education, and Welfare suggest a lower abuse potential for fenfluramine.

2. Fenfluramine will upon the approval of a new drug application by the FDA, have a currently accepted medical use in treatment in the United States.

3. Abuse of fenfluramine may lead to limited physical dependence relative to the drugs or other substances in schedule III.

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 § 308.14(b) of title 21 of the Code of Federal Regulations be amended to read:

§ 308.14 Schedule IV.

* * * * *

(c) *Fenfluramine.* Any material, compound, mixture, or preparation which contains any quantity of the following substances, 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:

(1) Fenfluramine, 1670.

* * * * *

Conferences have been held between the Bureau and the A. H. Robins Co., the only firm intending to market fenfluramine in the United States. The A. H. Robins Co. has fully cooperated with the Bureau and has consented to the placement of fenfluramine in schedule IV 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 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 I 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 3, 1973.

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

[FR Doc.73–9072 Filed 5–8–73;8:45 am]

[21 CFR Part 308]

SCHEDULES OF CONTROLLED SUBSTANCES

Proposed Placement of Mazindol 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, chlortermine, 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 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. SEGGEL,
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) materials submitted spontaneously to the Bureau by the manufacturer of mazindol regarding the abuse potential of this drug; (4) published scientific and medical literature from the United States and other nations regarding these drugs; (5) selected investigatory files compiled for law enforcement purposes by the Bureau and another law enforcement agency; and (6) the legislative history of the Controlled Substances Act.

The results of this review can be summarized as follows:

(1) Mazindol 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.

(2) Mazindol is covered by a new-drug application filed and pending with the Food and Drug Administration for use in treatment of obesity. The FDA has informed the Bureau that approval of this new-drug application is pending completion of certain administrative matters.

(3) 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.

(4) Mazindol has not been marketed in the United States or any other country, so there is no evidence of diversion or abuse.

(5) The House report on the Controlled Substances Act discusses the problem of determining the abuse potential of a drug which has not been marketed, by quoting from regulations promulgated under the Drug Abuse Control Amendment of 1965 (Comprehensive Drug Abuse Prevention and Control Act of 1970, House Report 91-1444 (part 1), p. 34, Sept. 10, 1970):

> 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:
>
> * * * * *
>
> (4) The drug or drugs containing such a substance are new drugs so related in their action to a drug or drugs already listed as having a potential for abuse to make it likely that the drug will have the same potentiality for abuse as such drugs, thus making it reasonable to assume that there may be significant diversions from legitimate channels, significant use contrary to or without medical advice, or that it has a substantial capability of creating hazards to the health of the user or to the safety of the community.

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. Because of the chemical and pharmacological similarities between mazindol and the other anorectic drugs being proposed for control, the Bureau is proposing placement of mazindol in schedule III. The Bureau will monitor the manufacture, distribution, and use of mazindol in the United States, paying special attention to indicators of diversion (such as shortages in accountability audits of distributors and dispensers, thefts from handlers, and availability on the illicit market) and to other indicators which indicate that mazindol is actually being abused (such as excessive prescribing and dispensing, reports of adverse reactions and overdoses, and other medical experiences). The Bureau will also consider, if available, clinical and other research in abusability, dependence-creating, and dependence-sustaining characteristics of mazindol. If, after 18 months during which the drug is marketed, experience suggests that mazindol has not been subject to significant diversion or abuse, the Director will review the necessity and desirability of maintaining mazindol in schedule III and will request from the Secretary of Health, Education, and Welfare a new scientific and medical evaluation, and his recommendation, as to whether mazindol should be so controlled or removed as a controlled substance. Any interested person may petition the Bureau to decontrol mazindol at any time.

Based upon the investigations and review of the Bureau of Narcotics and Dangerous Drugs and upon the scientific and medical evaluation and recommendation 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) and (b)), the Director of the Bureau of Narcotics and Dangerous Drugs finds that:

1. Based on information now available, mazindol has a potential for abuse less than the drugs or other substances currently listed in schedule II. Although 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 these properties is not substantial enough to warrant a finding that it has a potential for abuse equal to the stimulants in schedule II.

2. Mazindol will, upon the approval of a new-drug application by the Food and Drug Administration, have a currently accepted medical use in treatment in the United States.

3. Abuse of mazindol 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) Mazindol_____ 1605

* * * * *

Conferences have been held between the Bureau and Sandoz-Wander, Inc., the only firm intending to market mazindol in the United States. Sandoz-Wander has fully cooperated with the Bureau and 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 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.73-9068 Filed 5-8-73;8:45 am]

[21 CFR Part 308]

SCHEDULES OF CONTROLLED SUBSTANCES

Proposed Placement of Phendimetrazine 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, eDpartment 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 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 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. SEGGEL,
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) Phendimetrazine 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) Phendimetrazine 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) Phendimetrazine 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." (Comprensive Drug Abuse Prevention and Control Act of 1970, H. Rept. 91-1444 (pt. 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 of the community; or