

"(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 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 now available, phendimetrazine 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 phendimetrazine is not substantial enough to warrant a finding that it has a potential for abuse equal to the stimulants in schedule II.

2. Phendimetrazine has a currently accepted medical 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 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 § 309.33, 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 1629
- (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 has fully cooperated with the Bureau and has concurred in the placement of phendimetrazine 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 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 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 § 308.43 without a hearing.

Dated May 1, 1973.

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

[FR Doc.73-9069 Filed 5-8-73;8:45 am]

[21 CFR Part 308]  
 SCHEDULES OF CONTROLLED  
 SUBSTANCES

Proposed Placement of Phentermine 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 chlorpheniramine, 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 scanty 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. SEGCEL,  
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) Phentermine 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) Phentermine 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) Phentermine 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 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 now available, phentermine 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 phentermine is not substantial enough to warrant a finding that it has potential for abuse equal to the stimulants in schedule II.

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

3. Abuse of phentermine 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 Di-

rector 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) Phentermine..... 1040

Conferences have been held between the Bureau and the Dorsey Laboratories, Division of Sandoz-Warner, Inc., one of the two manufacturers of phentermine in the United States. Dorsey has fully cooperated with the Bureau and has consented to the placement of phentermine 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.73-9070 Filed 5-8-73;8:45 am]

**DEPARTMENT OF HEALTH,  
EDUCATION, AND WELFARE**

Food and Drug Administration  
[ 21 CFR Part 146e ]

**FEED GRADE BACITRACIN**

**Revision of Certification Requirements**

The Commissioner of Food and Drugs has received a petition from Commercial Solvents Corp., Terre Haute, Ind. 47808, requesting that the certification requirements specified by § 146e.427 (21 CFR part 146e) be revised. The section now provides cross reference to § 146e.425 (21 CFR part 146e) paragraphs (b), (c), and (d) for packaging, labeling, requests for certification, and samples. The cross-reference in effect, requires that the bacitracin used in the manufacture of bacitracin oral veterinary drugs certified under § 146e.427 be of pharmaceutical grade. The Commissioner of Food and Drugs has concluded that the bacitracins used in these oral veterinary preparations need not be of pharmaceutical grade for their safe and effective use.

Therefore, pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (sec. 512(n) (5), 82 Stat. 351; 21 U.S.C. 360b(n) (5)) and under authority delegated to the Commissioner (21 CFR 2.120), it is proposed that § 146e.427 be amended by revising paragraph (b), and by adding new paragraphs (c), as follows:

§ 146e.427 Feed grade bacitracin powder oral veterinary (crude bacitracin powder oral veterinary, unrefined bacitracin powder oral veterinary); feed grade zinc bacitracin powder oral veterinary (crude zinc bacitracin powder oral veterinary, unrefined zinc bacitracin powder oral veterinary).

\* \* \* \* \*

(b) *Labeling*.—Each package shall bear on its label or labeling, as hereinafter indicated, the following:

(1) On the outside wrapper or container and the immediate container:

(i) The batch mark.

(ii) The number of grams of bacitracin activity per pound, and the weight of the drug in the immediate container.

(iii) The statement "Expiration date \_\_\_\_\_", the blank being filled in with the date that is 18 months after the month during which the batch was certified, except that an expiration date of 24 months or 36 months may be used if the manufacturer has submitted to the Commissioner results of tests and assays showing that, after having been stored

for such period of time, such drug as prepared by him complies with the standards prescribed by paragraph (a) of this section.

(iv) The statement "For oral veterinary use only".

(v) If it is intended for use in animals raised for food production, it shall be labeled in accordance with the requirements of regulations in parts 121 and/or 135c of this chapter.

(2) On the circular or other labeling within or attached to the package, adequate directions and warnings for the veterinary use of such drug by the laity.

(c) Request for certification; samples.

(1) In addition to complying with the requirements of § 146.2 of this chapter, a person who requests certification of a batch shall submit with his request a statement showing the batch mark, the number of packages of each size in such batch, the batch mark and (unless it was previously submitted) the date on which the latest assay of the bacitracin used in making such batch was completed, the quantity of each ingredient used in making the batch, the date on which the latest assay of the drug comprising such batch was completed, and a statement that each other ingredient used conforms to the requirements prescribed therefor, by this section.

(2) Except as otherwise provided by subparagraph (4) of this paragraph, such person shall submit in connection with his request results of the tests and assays listed after each of the following, made by him on an accurately representative sample of:

(i) The batch. Grams of bacitracin per pound and moisture.

(ii) The bacitracin used in making the batch: Potency, moisture, and zinc content, if the bacitracin used is zinc bacitracin.

(3) Except as otherwise provided by subparagraph (4) of this paragraph, such person shall submit in connection with his request, in the quantities hereinafter indicated, accurately representative samples of the following:

(i) The batch: 1 immediate container for each 5,000 immediate containers in the batch, but in no case less than 6 immediate containers, unless each such container is packaged to contain more than 30 grams, in which case the sample shall consist of 30 grams for each 5,000 immediate containers in the batch, but in no case less than six 30-gram portions or more than twelve 30-gram portions. Such samples shall be collected by taking single immediate containers or 30-gram portions at such intervals throughout the entire time of packaging the batch that the quantities packaged during the intervals are approximately equal.

(ii) The bacitracin used in making the batch: one package consisting of a composite of six portions of approximately 1 gram each taken at random from different locations in the batch, packaged in accordance with the requirements of § 148.2 of this chapter.

(iii) In case of an initial request for certification, each other substance used in making the batch: 1 package of each containing approximately 5 grams.

(4) No result referred to in subparagraph (2) (ii) of this paragraph, and no sample referred to in subparagraph (3) (ii) of this paragraph, is required if such result or sample has been previously submitted.

Interested persons may, on or before July 9, 1973, file with the Hearing Clerk, Department of Health, Education, and Welfare, room 6-38, 5600 Fishers Lane, Rockville, Md. 20852, written comments (preferably in quintuplicate) regarding this proposal. Comments may be accompanied by a memorandum or brief in support thereof. Received comments may be seen in the above office during working hours, Monday through Friday.

Dated May 2, 1973.

SALT D. FINE,  
Associate Commissioner  
for Compliance.

[FR Doc.73-9146 Filed 5-8-73;8:45 am]

**[ 21 CFR Part 278 ]  
RECORDS AND REPORTS**

**Applicability of Requirements for Assemblers of Diagnostic X-ray Systems and Component Manufacturers**

The Commissioner of Food and Drugs is proposing to amend subpart H of the regulations, specifically § 278.701 (21 CFR 278.701), to set forth clearly the degree of applicability of certain record-keeping and reporting regulations to assemblers of diagnostic x-ray systems and component manufacturers. The amendments are proposed because final regulations pertaining to Performance Standards for Electronic Products, Diagnostic X-ray Systems and Their Major Components, published in the FEDERAL REGISTER of August 15, 1972 (37 FR 16461), to become effective August 15, 1973, introduced a distinction between assemblers and component manufacturers. The Commissioner is providing 60 days for comment on the proposed amendments and proposes to establish an effective date of August 15, 1973, for any final order.

The present wording of § 278.701(b) excludes manufacturers of listed products (§ 278.750) from meeting certain requirements of subpart H—Records and Reports, if such products are sold exclusively to other manufacturers for use as components of electronic products to be sold to purchasers, because generally when such components are exclusively sold in this manner, subsequent manufacturers are required to certify final products sold to purchasers.

The diagnostic x-ray system standard departs from this format in that it requires manufacturers to certify specified individual components, even when they are sold to subsequent manufacturers, including assemblers. In this case, however, assemblers of diagnostic x-ray