FDA agrees that the manufacturer must know how much preservative is contained in the orange juice as purchased. The agency concludes that the percent by weight of the preservative used, regardless of the amount, should be declared on the label as required by the present regulations and has so provided in the final regulation.

5. Two comments opposed the proposed label statement that "this food must be used only for further manufacturing." They asserted that this statement is unnecessary because these foods are generally packed in drums or barels to be used for further manufacturing and could not be sold at retail.

The agency agrees that if these foods are packed in drums or barrels, the proposed label statement is unnecessary. However, because of its concern over the possibility that the products could inadvertently be sold through retail channels if the two foods are packed in containers other than drums or barrels, FDA is requiring that when the foods are packed in containers whose capacities are less than 19 liters (5 gallons), the label shall bear a statement indicating that the foods are "for further manufacturing use only."

6. One comment stated that the proposed provision that would require each of the optional ingredients used to be declared on the label is unnecessary because the only ingredients present are orange juice or concentrated orange juice and preservative. The comment claimed that a statement of the percent by weight and name of the preservative used coupled with the name of the food is a complete list of ingredients, and suggested that any other listing would be redundant.

FDA agrees that if a preservative is the only optional ingredient used in these foods, the declaration of the preservative used along with the name of the food on the principal display panel constitutes a list of the optional ingredients used as required by 21 CFR Part 101. However, if concentrated orange juice with preservative (§ 146.154) contains a sweetener as permitted by the standard, then a listing of all optional ingredients used shall appear together on either the principal display panel or information panel of the label.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 401, 701(e), 52 Stat. 1046 as amended, 70 Stat. 919 as amended (21 U.S.C. 341, 371(e))) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 5.1), Part 146 is amended as follows:

1. In § 146.152 by revising paragraphs (b) and (d) to read as follows:

§ 146.152 Orange juice with preservative.

* * * * *

(b) The preservatives referred to in paragraph (a) of this section are any safe and suitable preservatives or combinations thereof.

* * * * *

(d) Each of the optional ingredients used shall be declared on the label as required by the applicable sections of Part 101 of this chapter. In addition, the name of each preservative shall be preceded by a statement of the percent by weight of the preservative used. If the food is packed in container sizes that are less than 19 liters (5 gallons), the label shall bear a statement indicating that the food is for further manufacturing use only.

* * * * *

2. In § 146.154 by revising paragraphs (b) and (d) to read as follows:

§ 146.154 Concentrated orange juice with preservative.

* * * * *

(b) The preservatives referred to in paragraph (a) of this section are any safe and suitable preservatives or combinations thereof.

* * * * *

(d) Each of the optional ingredients used shall be declared on the label as required by the applicable sections of Part 101 of this chapter. In addition, the name of each preservative shall be preceded by a statement of the percent by weight of the preservative used. If the food is packed in container sizes that are less than 19 liters (5 gallons), the label shall bear a statement indicating that the food is for further manufacturing use only.

* * * * *

Any person who will be adversely affected by the foregoing regulation may at any time on or before July 23, 1979, submit to the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857, written objections thereto and may make a written request for a public hearing on the stated objections. Each objection shall be separately numbered and each numbered objection shall specify with particularity the provision of the regulation to which objection is made. Each numbered objection on which a hearing is requested shall specifically so state; failure to request a hearing for any particular objection shall constitute a waiver of the right to a hearing on that objection. Each numbered objection for which a hearing is requested shall include a detailed description and analysis of the specific factual information intended to be presented in support of the objection in the event that a hearing is held; failure to include such a description and analysis for any particular objection shall constitute a waiver of the right to a hearing on the objection. Four copies of all documents shall be submitted and shall be identified with the Hearing Clerk docket number found in brackets in the heading of this regulation. Received objections may be seen in the above office between the hours of 9 a.m. and 4 p.m., Monday through Friday.

Effective date. Except as to any provisions that may be stayed by the filing of proper objections, compliance with this final regulation, including any required labeling changes, may begin July 23, 1979, and all products initially introduced into interstate commerce on or after July 1, 1981 shall fully comply. Notice of the filing of objections or lack thereof will be published in the Federal Register.

(Secs. 401, 701(e), 52 Stat. 1046 as amended, 70 Stat. 919 as amended (21 U.S.C. 341, 371(e)).)

Dated: June 13, 1979.

Joseph P. Hile,

Associate Commissioner for Regulatory Affairs.

[FR Doc. 79-19316 Filed 6-21-79; 8:45 am]

BILLING CODE 4110-03-M

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21 CFR Part 310

[Docket No. 75N-0244]

Drugs for Human Use; Over-the-Counter (OTC) Daytime Sedatives

AGENCY: Food and Drug Administration.

ACTION: Final order.

SUMMARY: This document contains the final decision that any ingredient when labeled for use as an over-the-counter (OTC) daytime sedative is not generally recognized as safe and effective for this intended use. Any product marketed for this use would be subject to regulatory action unless it is the subject of an approved new drug application. The Commissioner of Food and Drugs is taking this action after considering public comments on the tentative final order published in the Federal Register of June 13, 1978 (43 FR 25544). This final decision is part of FDA's ongoing review of OTC drug products.

EFFECTIVE DATE: December 24, 1979.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Bureau of Drugs (HFD–510), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301–443–4960.

SUPPLEMENTARY INFORMATION: In the Federal Register of December 8, 1975 (40 FR 57292), the agency, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), issued a proposal to establish monographs for OTC nighttime sleep-aid, daytime sedative, and stimulant drug products, together with the conclusions and recommendations of the Advisory Review Panel on OTC Sedative, Sleep-Aid, and Tranquilizer Drug Products.

In accordance with § 330.10(a)(2) (21 CFR 330.10(a)(2)), the data and information considered by the Panel were put on public display in the office of the Hearing Clerk, Food and Drug Administration (FDA), Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857, after deletion of trade secret information.

Tentative final orders pertaining to OTC nighttime sleep-aid and stimulant drug products were published in the Federal Register of June 13, 1978 (43 FR 25544). OTC daytime sedatives were discussed in the preamble to those orders but did not appear in a monograph included with the orders because all OTC daytime sedatives were placed in Category II as not generally recognized as safe and effective for OTC use. Interested persons were invited to file, within 60 days, written objections and to request an oral hearing before the Commissioner regarding the tentative final orders.

This order contains the agency's final decision on OTC daytime sedative drug products only. The agency's final decision on OTC nighttime sleep-aid and stimulant drug products will be discussed in future documents. Accordingly, only those comments and portions of comments addressed to the agency's conclusions on daytime sedatives (43 FR 25593) are discussed below. In response to the tentative final order, five comments were received from three consumers, one consumer group, and one manufacturer.

A. The Agency's Conclusions on the Comments

1. Comments from individual consumers expressed personal opinions in favor of or in opposition to the agency's decision to place daytime sedatives in Category II. The comment in favor of the decision stated that taking this action will reduce the number of drugs that are subject to abuse. The comments opposed to the decision stated that certain OTC daytime sedative products had provided relief for particular conditions (sleeplessness and headache) which are unrelated to the indications for a daytime sedative.

The comments opposed to the agency's decision to place OTC daytime sedatives in Category II provided personal testimony in support of specific OTC daytime sedative products but did not offer any reason to change the agency's decision. The agency reaffirms the conclusions stated in paragraph 68 of the preamble to the June 13, 1978 tentative final orders.

2. One comment urged FDA to take action outside the normal regulatory procedures to immediately remove scopolamine from OTC daytime sedative products because scopolamine is both unsafe and ineffective for this intended use.

The agency's policy with respect to ingredients in OTC drug products has been to take action outside the normal OTC regulatory process only when continued marketing of the ingredient poses a sufficient health hazard, e.g., halogenated salicylanilides. The agency stated in paragraph 71 of the preamble to the June 13, 1978 tentative final orders that the available data do not warrant initiating action outside the normal OTC drug review administrative process because the level of scopolamine contained in marketed OTC daytime sedative products is too low to warrant a serious safety concern. The comment provided no reason why the agency should reach a different conclusion at this time. In any case, according to the agency's information, since publication of the December 8, 1975 proposal many manufacturers of OTC daytime sedatives have reformulated their products to eliminate scopolamine. Moreover, publication of the final order contained in this document will require removal of all daytime sedatives, including any which still contain scopolamine, from the OTC market.

3. One comment stated that members of the OTC Sedative, Sleep-Aid, and Tranquilizer Panel were pressured by FDA officials to change, for legal reasons, the Panel's original recommendation that OTC daytime sedatives be placed in Category II. The comment demanded an investigation of such influence by FDA officials to seek full disclosure of those involved.

These same allegations were made in a hearing before the Subcommittee on Monopoly and Anticompetitive Activities of the Select Committee on Small Business, United States Senate, held in Washington, DC, on June 14 and 21, 1977. A copy of the record of those proceedings has been placed on public display in the agency's office of the Hearing Clerk, address given above. At the Senate hearing, one member of the OTC Sedative, Sleep-Aid, and Tranquilizer Panel stated that FDA officials pressured Panel members to "water down" the Panel's Category II recommendations by urging that daytime sedatives be placed in Category III because the available data did not support placing antihistamine products in Category II. This view was contradicted by the Panel Chairman, who wanted "to make it very clear that FDA did not exert any undue influence on the Panel, and certainly not on the Chairman." Another Panel member testified that, while disappointed with the Panel's majority decision to move daytime sedatives from Category II to Category III, the member "did not feel it was due to any undue pressures by the Chairman or the FDA." The agency therefore rejects the position asserted in the comment.

4. One comment requested a hearing to present objections to the agency's proposal to place methapyrilene-containing daytime sedatives in Category II. The comment merely stated "We herewith request a hearing before the Food and Drug Administration, in order to present our objections," but did not specify what the objections were.

Section 330.10(a)(7) of the regulations (21 CFR 330.10(a)(7)) states that any objections to a tentative final monograph are to be supported by a brief statement of the grounds for the objections and that a request for an oral hearing may accompany such objections. Section 330.10(a)(8) (21 CFR 330.10(a)(8)) states that the Commissioner will schedule an oral hearing if the grounds in support of the objections are reasonable. Because the person requesting a hearing did not give any statement of the grounds for the objections, and because the agency is unaware of any reasonable grounds that would justify a hearing on the issues relating to daytime sedatives, the hearing request is denied. Further, the agency and the drug industry are currently taking action to remove methapyrilene-containing drug products from the market in response to recent findings by the National Cancer Institute that methapyrilene is a carcinogen. Thus, the request for a hearing would serve no purpose.

B. The Agency's Final Conclusions on OTC Daytime Sedative Drug Products

Antihistamines, bromides, and scopolamine compounds, either singly or in combination with other ingredients, e.g., analgesics, amino acids, and vitamins, have been marketed for use as OTC daytime sedatives (or similar or related indications). The following claims were submitted for the daytime sedative products: "occasional simple nervous tension," "nervous irritability," "nervous headache," "simple nervousness due to common every day overwork and fatigue," "a relaxed feeling," "calming down and relaxing," "gently soothe away the tension," "calmative," and "resolving that irritability that ruins your day." The agency is also aware of the following claims that have been associated with these drugs: "helps you relax," "restlessness," "when you're under occasional stress . . . helps you work relaxed."

While antihistamine drugs, when used as daytime sedatives, make the user drowsy or sleepy, there are no data to indicate that the drowsiness effect is related to relieving symptoms of anxiety. Drowsiness is in fact an undesirable side effect for persons using these products during the day, when they need to be alert. Accordingly, the agency concludes that antihistamines should be classified in Category II because they are not generally recognized as safe or effective when used as daytime sedatives.

The bromide compounds are being placed in Category II because they do not act as daytime sedatives in a single dose and, if taken over a long enough period of time to reach therapeutic levels, could be severely toxic.

The scopolamine compounds are classified in Category II because they are ineffective at presently marketed doses. At higher doses that would achieve a therapeutic effect (drowsiness), the scopolamine compounds are unsafe because of the potential for toxic effects associated with these doses. In addition, as stated in the paragraph discussing antihistamines, drowsiness is unrelated to the desired therapeutic effect of daytime sedative products.

The agency is unaware of any OTC daytime sedative drug product that is the subject of an approved new drug application.

Based on the available evidence, the agency is making a final determination that no ingredient can be generally recognized as safe and effective for use as an OTC daytime sedative. If the labeling of any product represents or suggests it to be used as an OTC daytime sedative (or any similar or related indication) that product will be considered a new drug within the meaning of section 201 (p) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321(p)) and may not be marketed for this use unless it is the subject of an approved new drug application.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended, 1050–1053 as amended, 1055–1056 as amended (21 U.S.C. 321(p), 352, 355, 371)) and the Administrative Procedure Act (5 U.S.C. 553, 554, 702, 703, 704) and under authority delegated to the Commissioner (21 CFR 5.1), Subchapter D of Title 21 of the Code of Federal Regulations is amended by adding new § 310.519 to read as follows:

§ 310.519 Drug products marketed as over-the-counter (OTC) daytime sedatives.

(a) Antihistamines, bromides, and scopolamine compounds, either singly or in combinations, have been marketed as ingredients in over-the-counter (OTC) drug products for use as daytime sedatives. The following claims have been made for daytime sedative products: "occasional simple nervous tension," "nervous irritability," "nervous headache," "simple nervousness due to common every day overwork and fatigue," "a relaxed feeling," "calming down and relaxing," "gently soothe away the tension," "calmative," "resolving that irritability that ruins your day," "helps you relax," "restlessness," "when you're under occasional stress . . . helps you work relaxed." Based on evidence presently available, there are no ingredients that can be generally recognized as safe and effective for use as OTC daytime sedatives.

(b) Any OTC drug product that is labled, represented, or promoted as an OTC daytime sedative (or any similar or related indication) is regarded as a new drug within the meaning of section 201(p) of the Federal Food, Drug, and Cosmetic Act for which an approved new drug application under section 505 of the act and Part 314 of this chapter is required for marketing.

(c) A completed and signed "Notice of Claimed Investigational Exemption for a New Drug" (Form FD–1571), as set forth in § 312.1 of this chapter, is required to cover clinical investigations designed to obtain evidence that such a preparation is safe for the purpose intended.

(d) Any OTC daytime sedative drug product introduced into interstate commerce after December 24, 1979, that is not in compliance with this section is subject to regulatory action.

Effective date, This order will be effective December 24, 1979.

(Secs. 201(p), 502, 505, 701, 52 Stat. 1041–1042 as amended 1050–1053 as amended, 1055–1056 as amended (21 U.S.C. 321(p), 352, 355, 371) (5 U.S.C. 553, 554, 702, 703, 704).)

Dated: June 18, 1979.

Sherwin Gardner,

Acting Commissioner of Food and Drugs.

[FR Doc. 79–19448 Filed 6–21–79; 8:45 am]

BILLING CODE 4110–03–M

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21 CFR Part 520

Oral Dosage Form New Animal Drugs Not Subject to Certification; Pyrantel Pamoate Suspension

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The animal drug regulations are amended to reflect approval of a supplemental new animal drug application (NADA) filed by Pfizer, Inc., providing for safe and effective use of a higher concentration of a currently approved anthelmintic suspension for removal of roundworms and hookworms in dogs.

EFFECTIVE DATE: June 22, 1979.

FOR FURTHER INFORMATION CONTACT: Bob G. Griffith, Bureau of Veterinary Medicine (HFV–112), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301–443–3430.

SUPPLEMENTARY INFORMATION: Pfizer, Inc., 235 E. 42d St., New York, NY 10017, filed a supplemental NADA providing for use of a suspension of 4.54 milligrams of pyrantel (as pyrantel pamoate) per milliliter for removal of roundworms and hookworms in dogs. Pfizer currently holds approval for a suspension containing 2.27 milligrams of pyrantel base per milliliter. This supplemental dosage form covers only a change in concentration of active ingredient from 2.27 milligrams per milliliter to 4.54 milligrams per milliliter. No change is being made in the approved conditions of use, and no added risk of toxicity is present from the inadvertent overdosage of this new concentration. Therefore, under the Bureau's supplemental policy, the approval of this supplemental application has not required a reevaluation of the parent NADA.

In accordance with the freedom of information regulations and § 514.11(e)(2)(ii) of the animal drug