Proposed Rules

Federal Register
Vol. 45, No. 30
Tuesday, February 12, 1980

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 rule making prior to the adoption of the final rules.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

21 CFR Part 25

[Docket No. 79N-0335]

National Environmental Policy Act; Proposed Policies and Procedures; Extension of Comment Period

AGENCY: Food and Drug Administration.

ACTION: Extension of comment period.

SUMMARY: The agency is extending the comment period for submitting comments on the proposed policies and supplemental procedures for compliance with the National Environmental Policy Act (NEPA) and the Council on Environmental Quality's (CEQ) National Environmental Policy Act Regulations.

DATE: The comment period is extended to March 12, 1980.

ADDRESS: Written comments to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: Kenneth E. Taylor, Bureau of Veterinary Medicine (HFV-9), Food and Drug Administration, Department of Health, Education, and Welfare, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4500.

SUPPLEMENTARY INFORMATION: In the Federal Register of December 11, 1979 (44 FR 71742), FDA proposed policies and supplemental procedures for compliance with the NEPA and CEQ National Environmental Act Regulations. Comments on the proposal were due by February 11, 1980.

In a letter dated January 28, 1980, the Pharmaceutical Manufacturers Association (PMA), 1155 Fifteenth St. NW., Washington, DC 20005, requested that the comment period on the proposal be extended 30 days to provide additional time needed by PMA to properly ascertain the views of its membership on the proposal. In a letter dated January 29, 1980, the Animal Health Institute (AHI), Suite 1009, 1717 K St. NW., Washington, DC 20036, requested that the comment period on the proposal be extended 60 days to provide additional time for AHI to assure that provisions of FDA's proposal are fully mandated by the CEQ's regulations. Copies of both the PMA and AHI requests are on file with the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

FDA intends to issue a final rule based on this proposal as soon as possible. The agency has concluded that an extension of the comment period should be granted but that the extension should be limited to 30 days. Accordingly, the comment period is extended to March 12, 1980. Comments may be seen in the office of the Hearing Clerk at the address above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: February 5, 1980.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 80-4255 Filed 2-11-80; 8:45 am]

BILLING CODE 4110-03-M

21 CFR Parts 182 and 184

[Docket No. 78N-0272]

Phosphates; Proposed Affirmation of and Deletion From GRAS Status as Direct and Indirect Human Food Ingredients

Corrections

In FR Doc. 79-38647, published at page 74845, on Tuesday, December 18, 1979, make the following corrections:

1. The subject heading should be corrected to read as set forth above;

2. On page 74850, in the second column, in the thirteenth line of the second paragraph, "1.2, and 1.8 and 1.8 percent phosphorus," should be corrected to read "1.2, and 1.8 percent phosphorus,";

3. On page 74850, in the third column, in the second paragraph:

a. In the eighth line "(Ca:P ratio, 1:31) . . ." should be corrected to read "(Ca:P ratio, 1:3.1) . . .";

b. In the thirteenth line "calification" should be corrected to read "calcification";

4. On page 74854, in the second column, in paragraph (a) under § 184.1214, in the eleventh line "liquid" should be corrected to read "liquor";

5. On page 74856, in the first column, in the second paragraph, paragraph (d), after the third line, add the following: "in accordance with § 184.1(b)(i). Current good manufacturing practice";

6. On page 74857:

a. In the second column, in the first paragraph, paragraph (c), delete the fourth and fifth lines, add the word "in" to the beginning of the sixth line, and in the seventh line "agent as defined in § 170.3(o)(24) of this" should be corrected to read "agent as defined in § 170.3(o)(23) of this chapter, processing aid as defined in § 170.3(o)(24) of this";

b. In the second column, in paragraph (c) under § 184.1810, in the fifth line "§ 170.3(11)" should be corrected to read "§ 170.3(o)(11)";

c. In the second column, in paragraph (c) under § 184.1810, in the ninth line the word "in" should be added to the end of the line;

d. In the third column, in the first paragraph, paragraph (d), in the tenth line ". . . chapter 0.5 percent" should be corrected to read ". . . chapter, 0.5 percent";

e. In the third column, in the first paragraph, paragraph (d), in the twelfth line "§ 170.3(n)" should be corrected to read "§ 170.3(n)(26)";

f. In the third column, in the second line of paragraph (a) under § 184.1872, "($Na_5 P_2 O_7$ CAS Reg. No. 007722-88-5)" should be corrected to read "($Na_4 P_2 O_7$ CAS Reg. No. 007722-88-5)".

BILLING CODE 1505-01-M

21 CFR Part 357

[Docket No. 79N-0368]

Cholecystokinetic Drug Products for Over-the-Counter Human Use; Establishment of a Monograph; Proposed Rulemaking

AGENCY: Food and Drug Administration.

ACTION: Proposed rule.

SUMMARY: This proposed rule would establish conditions under which over-the-counter (OTC) cholecystokinetic drug products (products which cause contraction of the gallbladder during diagnostic gallbladder studies) are generally recognized as safe and effective and not misbranded. The proposed rule, based on the recommendations of the Advisory

Review Panel on OTC Miscellaneous Internal Drug Products, is part of the ongoing review of OTC drug products conducted by the Food and Drug Administration (FDA).

DATES: Comments by May 12, 1980; reply comments by June 11, 1980.

ADDRESSES: Written comments to the Hearing Clerk (HFA–305), Food and Drug Administration, Rm. 4–65, 5600 Fishers Lane, Rockville, MD 20857.

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 accordance with Part 330 (21 CFR Part 330), FDA received on June 23, 1978, a report of the Advisory Review Panel on OTC Miscellaneous Internal Drug Products. Under § 330.10(a)(6) (21 CFR 330.10(a)(6)), the Commissioner of Food and Drug issues (1) a proposed regulation containing the monograph recommended by the Panel, which establishes conditions under which OTC drugs are generally recognized as safe and effective and not misbranded (i.e., Category I); (2) a statement of the conditions excluded from the monograph because the Panel determined that they would result in the drugs not being generally recognized as safe and effective or would result in misbranding (i.e. Category II); (3) a statement of the conditions excluded from the monograph because the Panel determined that the available data are insufficient to classify these conditions under either (1) or (2) above (i.e., Category III); and (4) the conclusions and recommendations of the Panel. The Panel's conclusions on cholecystokinetic drug products contained no Category II or Category III conditions.

The unaltered conclusions and recommendations of the Panel are issued to stimulate discussion, evaluation, and comment on the full sweep of the Panel's deliberations. The report has been prepared independently of FDA, and the agency has not yet fully evaluated the report. The Panel's findings appear in this document as a formal proposal to obtain public comment before the agency reaches any decision on the Panel's recommendations. This document represents the best scientific judgment of the Panel members but does not necessarily reflect the agency's position on any particular matter contained in it. After FDA has carefully reveiwed all comments submitted in response to this proposal, the Commissioner will issue a tentative final regulation in the Federal Register to establish a monograph for OTC cholecystokinetic drug products.

In accordance with § 330.10(a)(2)(21 CFR 330.10(a)(2)), the Panel and FDA have held as confidential all information concerning OTC cholecystokinetic drug products submitted for consideration by the Advisory Review Panel. All this information will be put on public display at the office of the Hearing Clerk, Food and Drug Administration, after March 13, 1980, except to the extent that the person submitting it demonstrates that it still falls within the confidentiality provisions of 18 U.S.C. 1905 or section 301(j) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 331(j)). Requests for confidentiality should be submitted to William E. Gilbertson, Bureau of Drugs (HFD–510) (address given above).

Based upon the conclusions and recommendations of the Panel, FDA proposes that the conditions included in the monograph, under which the drug products would be generally recognized as safe and effective and not misbranded (Category I), be effective 30 days after the date of publication of the final monograph in the Federal Register.

A proposed review of the safety, effectiveness, and labeling of all OTC drugs by independent advisory review panels was announced in the Federal Register of January 5, 1972 (37 FR 85). The final regulations providing for this OTC drug review under § 330.10 were published and made effective in the Federal Register of May 11, 1972 (37 FR 9464). In accordance with these regulations, a request for data and information on all active ingredients used in OTC miscellaneous internal drug products was issued in the Federal Register of November 16, 1973 (38 FR 31696). In the Federal Register of August 27, 1975 (40 FR 38179), an additional notice supplemented the initial notice with a detailed list of ingredients contained in OTC miscellaneous drug products.

The Commissioner appointed the following Panel to review the information submitted and to prepare a report under § 330.10(a) (1) and (5) on the safety, effectiveness, and labeling of the ingredients in those products: John W. Norcross, M.D., Chairman, Ruth Eleanor Brown, R. Ph. (resigned May 1976), Elizabeth C. Giblin, Ed. D., Richard D. Harshfield, M.D., Theodore L. Hyde, M.D., Claus A. Rohweder, D.O., Samuel O. Thier, M.D. (resigned November 1975), William R. Arrowsmith, M.D. (appointed March 1976), Diana F. Rodriguez-Calvert, Pharm. D. (appointed July 1976).

Representatives of consumer and industry interests served as nonvoting members of the Panel. Eileen Hoates, nominated by the Consumer Federation of America, served as the consumer liaison until September 1975, followed by Michael Schulman, J.D. Francis J. Haley, M.D., served as the industry liaison, and in his absence John Parker, Pharm. D., served. Dr. Hailey served until June 1975, followed by James M. Holbert, Sr., Ph. D. All industry liaison members were nominated by the Proprietary Association.

The following FDA employees assisted the Panel: Armond M. Welch, R. Ph., served as the Panel Administrator. Enrique Fefer, Ph. D., served as the Executive Secretary until July 1976, followed by George W. James, Ph. D., until October 1976, followed by Natalia Morgenstern until May 1977, followed by Arthur Auer. Joseph Hussion, R. Ph., served as the Drug Information Analyst until July 1976, followed by Anne Eggers, R. Ph., M.S., until October 1977, followed by John R. Short, R. Ph.

In order to expand its medical and scientific base, the Panel called upon a consultant in statistics, Ralph B. D'Agostino, Ph. D., for advice.

The Advisory Review Panel on OTC Miscellaneous Internal Drug Products was charged with the review of many categories of drugs. Because of the large number of ingredients and varied labeling claims, the Panel decided to review and publish its findings separately for several drug categories and individual drug products. The Panel presents its conclusions and recommendations for cholecystokinetic drug products in this document. The review of all other categories of miscellaneous internal drug products will be continued by the Panel, and its findings will be published periodically in future issues of the Federal Register.

The Panel was first convened on January 13, 1975 in an organizational meeting. Working meetings were held on the following dates (the dates of those meetings which dealt with the topic of this document are in italics): February 23 and 24, March 23 and 24, April 27 and 28, *June 22 and 23,* September 21 and 22, and November 16 and 17, 1975; February 8 and 9, March 7 and 8, April 11 and 12, May 9 and 10, July 11 and 12, and October 10 and 11, 1976; February 20 and 21, April 3 and 4, May 15 and 16, *July 9, 10, and 11,* October 15, 16, and 17, and December 2, 3, and 4, 1977; January 28, 29, and 30, March 10, 11, and 12, *May 5, 6, and 7,* and *June 23, 1978.*

The minutes of the Panel meetings are on public display in the office of the Hearing Clerk (HFA–305), Food and Drug Administration (address given above). No person requested an

opportunity to appear before the Panel to express his or her views on cholecystokinetic drug products.

The Panel has thoroughly reviewed literature and the one data omission and has considered all pertinent data and information submitted through June 23, 1978 in arriving at its conclusions and recommendations.

In accordance with the OTC drug review regulations (21 CFR 330.10), the Panel considered OTC cholecystokinetic drug products with respect to the following three categories:

Category I. Conditions under which OTC cholecystokinetic drug products are generally recognized as safe and effective and are not misbranded.

Category II. Conditions under which OTC cholecystokinetic drug products are not generally recognized as safe and effective and are misbranded.

Category III. Conditions for which the available data are insufficient to permit final classification at this time.

A. Submission of Data and Information

Pursuant to the notices published in the Federal Register of November 16, 1973 (38 FR 31696) and August 27, 1975 (40 FR 38179) requesting the submission of data and information on OTC miscellaneous internal drug products, the following firm made a submission related to a product for use as a olecystokinetic.

ubmissions by Firms

Firm: Grey Pharmaceutical Co., Norwalk, CT 06856; Marketed product: G.B. Prep.

2. Classification of Ingredients

The active ingredient in the cholecystokinetic, G.B. Prep., is an aqueous emulsion of corn oil.

B. Referenced OTC Volume

The "OTC Volume" cited in this document is the submission made in response to the call-for-data notices published in the Federal Register of November 16, 1973 (38 FR 31696) and August 27, 1975 (40 FR 38179). All of the information included in this volume, except for any deletions which were made in accordance with the confidentiality provisions set forth in § 330.10(a)(2), will be put on public display after March 13, 1980, in the office of the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857.

C. General Discussion

A cholecystokinetic drug product causes contraction of the gallbladder l is used during the course of diagnostic gallbladder studies (cholecystography). Patients may be advised by a physician to obtain this drug and use it at a given time in preparation for the diagnostic procedure. The Panel concludes that such a preparation should be available to the consumer without a prescription because it is a safe and effective agent in preparation for cholecystography.

D. Category I Conditions for Cholecystokinetic Drug Products

The following are Category I conditions under which drug products used for the contraction of the gallbladder during cholecystography are generally recognized as safe and effective.

1. *Category I active ingredient—aqueous emulsion of corn oil.* The Panel concludes that corn oil is safe and effective in the recommended single dose of two ounces (¼ cup) of a 50-percent aqueous emulsion when used as a cholecystokinetic agent in cholecystography.

a. *Safety.* Corn oil has been used for many years as an ingredient in food products such as salad dressings and margarines without reported evidence of harmful effects.

b. *Effectiveness.* In radiologic techniques, emulsified corn oil, when given in the above dosage, acts as a "fatty meal" causing a previously opacified gallbladder to rapidly contract. It is believed that corn oil reaching the upper small intestine causes the hormone cholecystokinin to be released from the small intestinal mucosa into the blood stream and hence to the gallbladder stimulating it to contract vigorously (Ref. 1).

c. *Dosage.* The Panel recommends that corn oil be adminstered orally in a single, two-once dose of a 50-percent aqueous emulsion.

D. *Labeling.* The Panel recommends the Category I labeling for OTC cholecystokinetic drug products. (See paragraph D.2. below—Category I labeling.)

2. *Category I labeling.* The Panel recommends the following labeling to be generally recognized as safe and effective and not misbranded for cholecystokinetic drug products:

a. *Indications.*

(1) "For contraction of the gallbladder during cholecystography."

(2) "For visualization of biliary ducts during cholecystography."

b. *Directions.*

(1) "Take only when instructed by a physician."

(2) "Shake well before using."

Reference

(1) Best, C. H., and N. B. Taylor, "The Physiologic Basis of Medical Practice," 7th Ed., Williams and Wilkins, Baltimore, p. 659, 1961.

The Food and Drug Administration has determined that this document is exempt from the requirement of preparing an Environmental Imapct Statement as specified under 21 CFR 25.1(f)(4).

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 210, 502, 505, 701, 52 Stat. 1040–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321, 352, 355, 371)), and the Administrative Procedure Act (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704)), and under authority delegated to the Commissioner (21 CFR 5.1), it is proposed that Subchapter D of Chapter I of Title 21 of the Code of Federal Regulations be amended by adding to Part 357 new Subpart C, to read as follows:

Subpart C—Cholecystokinetic Drug Products

Sec.

Authority: Secs. 201 502, 505, 701, 52 Stat. 1040–1042 as amended, 1050–1053 as amended, 1055–1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321, 352, 355, 371); (5 U.S.C. 553, 554, 702, 703, 704).

Subpart C—Cholecystokinetic Drug Products

§ 357.201 Scope.

An over-the-counter cholecystokinetic drug product in a form suitable for oral administration is generally recognized as safe and effective and is not misbranded if it meets each of the conditions in this Part 357, Subpart C, in addition to each general condition established in § 330.1 of this chapter.

§ 357.203 Definition.

Cholecystokinetic drug product. A drug product which causes contraction of the gallbladder and is used during the course of diagnostic gallbladder studies (cholecystography).

§ 357.210 Cholecystokinetic active ingredient.

The active ingredient of the product consists of the following when used within the dosage limits established.

Aqueous emulsion (50 percent) of corn oil.

§ 357.250 Labeling of cholecystokinetic drug products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug, if any, and identifies the product as a "cholecystokinetic."

(b) *Indications.* The labeling of the product contains a statement of the indications under the heading "Indications" that reads:

(1) "For the contraction of the gallbladder during cholecystography."

(2) "For visualization of biliary ducts during cholecystography."

(c) *Directions.* The labeling of the product contains the following statements under the heading "Directions":

(1) "Take only when instructed by a physician."

(2) "Shake well before using."

Interested persons are invited to submit their comments in writing (perferably in four copies and identified with the Hearing Clerk docket number found in brackets in the heading of this document) regarding this proposal on or before May 12, 1980. Comments should be addressed to the Hearing Clerk (HFA-305), Food and Drug Administration, Rm. 4-65, 5600 Fishers Lane, Rockville, MD 20857, and may be accompanied by a supporting memorandum or brief. Comments replying to comments may also be submitted on or before June 11, 1980. Comments may be seen in the above office between 9 a.m. and 4 p.m., Monday through Friday.

In accordance with Executive Order 12044, the economic effects of this proposal have been carefully analyzed, and it has been determined that the proposed rulemaking does not involve major economic consequences as defined by that order. A copy of the regulatory analysis assessment supporting this determination is on file with the Hearing Clerk, Food and Drug Administration.

Dated: February 5, 1980.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 80-4256 Filed 2-11-80; 8:45 am]

BILLING CODE 4110-03-M

DEPARTMENT OF JUSTICE

Drug Enforcement Administration

21 CFR Part 1312

Proposed Limitations on Import of Narcotic Raw Materials

AGENCY: Drug Enforcement Administration, Justice.

ACTION: Notice of proposed rulemaking on narcotic importation policy.

SUMMARY: This is a notice of proposed rulemaking issued by the Administrator of the Drug Enforcement Administration (DEA), to implement a narcotic importation policy in support of a worldwide effort to avoid the proliferation of sources for export of narcotic raw materials. The Administrator has decided to amend section 1312 of Title 21, Code of Federal Regulations, in accordance with the policy as pronounced in the advanced notice of proposed rulemaking, published in the Federal Register on June 12, 1979. (44 FR 33695).

DATES: Written comments or requests for a hearing should be received on or before April 14, 1980.

ADDRESS: Send comments to: Administrator, Drug Enforcement Administration, U.S. Department of Justice, 1405 I Street, NW., Washington, D.C. 20537, Attention: DEA Federal Register Representative.

FOR FURTHER INFORMATION CONTACT: William M. Lenck, Chief Counsel, Drug Enforcement Administration, telephone (202) 633-1276.

SUPPLEMENTARY INFORMATION: The background of the proposed policy is set forth in the advanced notice of proposed rulemaking on narcotic importation policy, *supra.* Adoption of the proposed policy, as outlined in the advanced notice will assist in eliminating the fundamental cause of excess supply of narcotic raw materials—the proliferation of sources for export—thereby, lessening the danger that excess supplies will be diverted to illicit traffic. the proposed policy's limitations on U.S. imports will discourage numerous countries from cultivating *Papaver somniferum* poppies for export of opium, poppy straw or concentrate of poppy straw from such poppies.

Interested persons have been afforded an opportunity to comment on the proposed policy by an advanced notice of proposed rulemaking, supra, and due consideration has been given to all comments received in response to the notice, insofar as they relate to the scope of the notice.

Discussion of Comments

The Department of State has furnished its unqualified support of the proposed policy as outlined in the Advanced Notice of Proposed Rulemaking (ANPR).[1] Briefly, it considers the ANPR a needed response from the United States to promote balance between worldwide supply and demand of narcotic raw materials, thereby lessening the possibility that excess supplies will be diverted into illicit traffic.

Other favorable comments have been received in support of the proposed policy which need not be repeated in this notice. Nevertheless, there were several comments filed primarily on behalf of parties adversely affected by the ANPR which objected to the proposed policy. These objections require separate DEA responses.

One commentator has suggested that resolution 471[2] should be interpreted to limit markets to those supplier countries which the world has relied upon for narcotic raw materials over the last decade. Another commentator has argued that to support the traditional supply countries cannot mean that purchases of narcotic raw materials from non-traditional suppliers should be totally prohibited. Nevertheless, the Commission on Narcotic Drugs, during its 1979 session, specifically rejected language in resolution 471 which would substitute "existing suppliers" in place of "traditional suppliers". The intent of the resolution to discourage new producers was clear. The United States, by generally relying only upon those countries authorized by international convention to produce opium for export, has not misinterpreted the intent of resolution 471.

Certain commentators have suggested that the proposed policy will not solve the problem of oversupply of narcotic raw materials. They have attributed the oversupply to the increase in production of traditional nations, not the proliferation of supplier countries. Moreover, they have not viewed the oversupply a threat for diversion of narcotics into the illicit market. However, the consensus shared by the international community has been that the cause of overproduction of narcotic raw materials is the proliferation of suppliers. In addition, although DEA has no evidence of diversion of licit supplies, its considers the International Narcotics Control Board's forecast of future oversupplies a threat which requires preventive action.

Several commentators have been concerned that the proposed policy has failed to assure adequate supplies of essential drugs. They have claimed that the recent pledges of Australia, France, Turkey and India to reduce acreage of cultivation, the potential climatic hazards of India and Turkey, the specter

[1] Copies of the full texts of the State Department position are provided in the appendix of this notice.

[2] The full text of resolution 471, as adopted by the Commission on Narcotic Drugs, is reprinted in the ANPR, *supra.*