The Proposed Amendment

In consideration of the foregoing, the Federal Aviation Administration proposes to amend 14 CFR part 71 as follows:

PART 71—[AMENDED]

1. The authority citation for 14 CFR part 71 continues to read as follows:

Authority: 49 U.S.C. app. 1348(a), 1354(a), 1510; E.O. 10854, 24 FR 9565, 3 CFR, 1959–1963 Comp., p. 389; 49 U.S.C. 106(g); 14 CFR 11.69.

§ 71.1 [Amended]

2. The incorporation by reference in 14 CFR 71.1 of the Federal Aviation Administration Order 7400.9A, Airspace Designations and Reporting Points, dated June 17, 1993, and effective September 16, 1993, is amended as follows:

Paragraph 6005 Class E airspace areas extending upward from 700 feet or more above the surface of the earth

* * * * *

ASW TX E5 Clarendon, TX [Modify]

Clarendon Municipal Airport, TX.
(lat. 34°54'38" N., long. 100°52'12" W.)
Clarendon RBN
(lat. 34°54'37" N., long. 100°52'05" W.)

That airspace extending upward from 700 feet above the surface within a 6.5-mile radius of Clarendon Municipal Airport and within 1.3 miles each side of the 209° bearing from the Clarendon RBM extending from the airport to 7.4 miles southwest of the RBN.

* * * * *

Larry D. Gray,

Acting Manager, Air Traffic Division, Southwest Region.

[FR Doc. 94–7655 Filed 3–30–94; 8:45 am]

BILLING CODE 4910–13–M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 334

[Docket No. 78N–036L]

RIN 0905–AA06

Laxative Drug Products for Over-The-Counter Human Use; Proposed Amendment to the Tentative Final Monograph

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of proposed rulemaking.

SUMMARY: The Food and Drug Administration (FDA) is amending the tentative final monograph for over-the-counter (OTC) laxative drug products to limit the OTC container size for sodium phosphate/sodium biphosphate oral solution to not greater than 90 milliliters (mL) (3 ounces (oz)). FDA is limiting this container size because of reports of deaths associated with an overdosage of sodium phosphate/sodium biphosphate oral solution where the product was packaged in a larger-size container and a larger than intended dose was taken inadvertently. The agency is also adding a warning for all sodium phosphate/sodium biphosphate products not to exceed the recommended dosage unless directed by a doctor. This proposal is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Written comments on the proposed regulation by May 31, 1994; written comments on the agency's economic impact determination by May 31, 1994. FDA is proposing that this portion of the final monograph be effective 30 days after the date of publication of the final rule in the **Federal Register.**

ADDRESSES: Written comments to the Dockets Management Branch (HFA–305), Food and Drug Administration, rm. 1–23, 12420 Parklawn Dr., Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: William E. Gilbertson, Center for Drug Evaluation and Research (HFD–810),Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–594–5000.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of March 21, 1975 (40 FR 12902), FDA published, under § 330.10(a)(6) (21 CFR 330.10(a)(6)), an advance notice of proposed rulemaking to establish a monograph for OTC laxative, antidiarrheal, emetic, and antiemetic drug products, together with the recommendations of the Advisory Review Panel on OTC Laxative, Antidiarrheal, Emetic, and Antiemetic Drug Products (the Panel), which was the advisory review panel responsible for evaluating data on the active ingredients in these classes. The Panel recommended monograph status for phosphate salts, such as sodium phosphate/sodium biphosphate oral solution (40 FR 12902 at 12940), but did not recommend any container size limitations.

The agency's proposed regulation, in the form of a tentative final monograph, for OTC laxative drug products was published in the **Federal Register** of January 15, 1985 (50 FR 2124). The agency also proposed monograph status for sodium phosphate/sodium biphosphate oral solution (50 FR 2124 at 2152 and 2155), but did not recommend any container size limitations. The proposed dosage for adults and children 12 years of age and over is 3.42 to 7.56 grams (g) of sodium phosphate and 9.1 to 20.2 g of sodium biphosphate in a single daily dose. In addition to its use as an OTC laxative for the relief of occasional constipation, sodium phosphate/sodium biphosphate oral solution is used as part of a bowel ansing regimen in preparing a patient for surgery or for preparing the colon for x-ray endoscopic examination. (See proposed § 334.80(a)(2), 50 FR 2124 at 2157.)

The major trade product containing sodium phosphate/sodium biphosphate oral solution is marketed in 45 mL, 90-mL, and 240-mL bottles (Ref. 1). The purgative dose or dose used for colonoscopy is 45 mL (1 1/2 oz). Because the product is available in three sizes, the manufacturer's labeling advises physicians to prescribe by volumes and not to prescribe by the bottle and not to exceed the recommended dosage, as serious side effects may occur (Ref. 1). Despite this labeling, the multiple container sizes available in the marketplace have caused consumer confusion and appear to have been involved in several consumer deaths.

II. Adverse Reactions and Deaths Associated with Sodium Phosphate/Sodium Biphosphate Oral Solution

From January 8, 1987, to April 21, 1993, the agency has received 5 reports of death in elderly patients and 13 reports of other adverse reactions related to the use of laxative drug products containing sodium phosphate/sodium biphosphate oral solution (Refs. 2 through 6). The five deaths involved elderly patients consuming the product in preparation for x-ray or endoscopic examinations. The first death (Ref. 2) involved a 72-year-old woman who apparently was instructed to take two sodium phosphate/sodium biphosphate enemas, but instead ingested 1 2/3 containers (size not known) of sodium phosphate/sodium biphosphate oral solution on the morning of her scheduled testing. She experienced cardiac arrest 1 hour after being admitted to the hospital and died within 9 hours after consuming the laxative. The second death (Ref. 2) involved an elderly male who was instructed by his radiologist to purchase sodium phosphate/sodium biphosphate oral solution to prepare for a barium enema. The patient purchased a 240-mL (8-oz) container and ingested the entire contents, apparently without following

the directions on the label. The patient soon developed severe diarrhea and collapsed, having no discernible pulse when the rescue squad arrived. The patient was hospitalized for symptoms of hyperphosphatemia and hypocalcemia and died within 48 hours after consuming the sodium phosphate/sodium biphosphate oral solution. Laboratory analyses 1 week prior to death revealed normal electrolyte values. The third death (Ref. 2) also involved an elderly male who was instructed by his physician to purchase sodium phosphate/sodium biphosphate oral solution in preparation for a colonoscopy. The physician was unaware that the solution was available in containers larger than 90 mL and had instructed the patient to drink one-half of the container in the morning and to take the second-half of the container later in the afternoon. The patient purchased the 240-mL container size and ingested the entire contents. The patient subsequently developed nausea, vomiting, and chills, followed by grand mal seizures, and was taken to the hospital after being found unconscious at home. Upon admission, the patient was treated for hyperphosphatemia and hypocalcemia, but did not respond to electrolyte replacement therapy. During hospitalization, the patient had several seizures, was placed on hemodialysis, eventually developed adult respiratory distress syndrome, and died. Overdosage of sodium phosphate/sodium biphosphate oral solution was considered the contributing factor to this patient's death. The fourth death occurred in an 80-year-old female nursing home patient (Ref. 3). The physician had ordered a 45 mL dose of sodium phosphate/sodium biphosphate oral solution to be given in preparation for an endoscopy exam. The nurse inadvertently gave the patient a 240-mL dose, and the patient died the next day. A fifth death involved a 71-year-old female (Ref. 4) admitted to the hospital for rectal prolapse corrective surgery. The patient's physician ordered a one-time dose of 240 mL of sodium phosphate/sodium biphosphate oral solution for the purpose of cleansing the patient's bowel prior to surgery. The pharmacist who filled the order questioned the dose and notified the patient's nurse that 240 mL appeared to be an unusual dose. The nurse discussed the dosage with the patient's physician, and the nurse was told to administer the entire 240 mL in one dose. The patient received the entire dose and died 2 hours later.

Four of the other reports of adverse reactions also involved serious cases of accidental overdosage. The first (Ref. 2) involved a 64-year-old male who consumed 240 mL of sodium phosphate/sodium biphosphate oral solution instead of the recommended dose of 45 mL. After realizing his mistake, the man notified his pharmacist and physician and was taken to an emergency room where his stomach was pumped. The second (Ref. 2) involved an elderly male (age not given) who consumed 300 mL of sodium phosphate/sodium biphosphate oral solution in preparation for a barium enema and experienced intestinal distress. The third (Ref. 5) was from a physician who instructed a patient to ingest 180 to 240 mL of sodium phosphate/sodium biphosphate enema solution in preparation for a colonoscopy (no details were given regarding the patient's response to this dose). The report stated that the enema was administered orally because the physician believed that the enema could be used instead of the oral solution. The fourth (Ref. 6) involved an elderly woman (age not given) who had consumed 120 mL of sodium phosphate/sodium biphosphate oral solution for treatment of constipation. After 1 hour, she did not obtain her desired laxation effect and she took another dose of 120 mL. She required hospitalization for treatment of an episode of calcium tetany.

Other reports of death have appeared in the literature. McConnell (Ref. 7) reported the death of a 48-year-old female who ingested sodium phosphate/sodium biphosphate oral solution daily in large doses. (The container size was not provided in the report.) The patient developed severe hypotension, became semicomatose, and did not respond to replacement electrolyte therapy for treatment of hypocalcemia and hyperphosphatemia. Postmortem examination of the lungs revealed congestion and edema. Although the kidneys showed hydropic degeneration of the renal tubules, it was unclear whether this lesion was present before the episode or was an organ complication from the overdosage of the laxative solution. Wiberg, Turner, and Nuttall (Ref. 8) reported a similar case of death caused by sodium phosphate/sodium biphosphate oral solution. A male patient with a previously normal serum calcium was admitted to the hospital for treatment of hypocalcemia after taking sodium phosphate/sodium biphosphate oral solution to clean the bowel of fecal material in preparation for a barium enema. However, the dose of the laxative was not provided. As a consequence of the electrolyte imbalance, the patient developed seizures and subsequently contracted aspiration pneumonia and soon died.

III. The Agency's Tentative Conclusions on Container Size Limitations for Sodium Phosphate/Sodium Biphosphate Oral Solution

Sodium phosphate/sodium biphosphate oral solution is considered safe when taken in the recommended dosage. The 45-mL and 90-mL container sizes are often recommended and prescribed by physicians for bowel cleansing purposes prior to surgery and diagnostic procedures of the colon. However, consumer and health professional confusion with resulting deaths have occurred as the result of the availability of a 240-mL container size. Unfortunately, life-threatening and fatal adverse reactions have occurred following inappropriate or erroneous ingestion of large amounts of this product. Following an overdose, particularly in the elderly, a high likelihood exists for hypernatremia (excessive amount of sodium in the blood) and hypocalcemia (reduction of blood calcium below normal), as well as other fluid and electrolyte imbalance. The reported cases (Refs. 2 through 6) illustrate the serious and acute serum electrolyte imbalances created by ingestion of large amounts of a sodium phosphate/sodium biphosphate oral solution. Phosphorus-calcium imbalances are aggravated by the copious colonic secretion of water, and are usually associated with a concomitant secretion of potassium. The secondary severe hypocalcemia may lead to heart block and tachyarrhythmias, which may cause sudden death.

The agency tentatively concludes that the OTC availability of the 240-mL container of sodium phosphate/sodium biphosphate oral solution creates a potential safety risk, particularly for elderly persons who are likely to use the product for bowel cleansing prior to surgery or a diagnostic procedure involving the colon. Because of the reported cases of accidental overdosing and the confusion that has occurred between 240-mL and 90 mL container sizes, the agency concludes that the 240-mL-size container of sodium phosphate/sodium biphosphate oral solution should no longer remain in the OTC marketplace. In the interest of safety, the agency is proposing to limit the maximum OTC container size for this product to 90 mL.

Based on the above, the agency is proposing to add new § 334.25 *Package size limitation* to the tentative final monograph. This new section will limit

the OTC containers of sodium phosphate/sodium biphosphate oral solution to a maximum of 90 mL. This container size will provide enough laxative to use for bowel cleansing prior to surgery or a diagnostic procedure involving the colon. Manufacturers will continue to be able to market a 45-mL container.

The agency proposes that any final rule that may issue based upon this proposal become effective 30 days after the date of publication of the final rule in the **Federal Register**. However, the agency does not believe that manufacturers should delay implementation until the OTC laxative drug products rulemaking is completed. Manufacturers of OTC laxative drug products are encouraged to comply voluntarily as soon as possible after the date of publication of this proposal.

The agency is currently aware of only one major trade product of sodium phosphate/sodium biphosphate oral solution available for OTC use. The manufacturer of this product recently ceased manufacture and shipment and instituted a market withdrawal of its 240-mL-size container of this product (Ref. 9). The agency is not currently aware of any other manufacturers with sodium phosphate/sodium biphosphate oral solution products in the marketplace. However, any other manufacturers of these products in container sizes greater than 90 mL are encouraged to also voluntarily cease manufacture and shipment and to withdraw them from the marketplace at this time.

The following information has been placed on display in the Dockets Management Branch (address above) and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

References

(1) "Physicians' Desk Reference," 47th ed., Medical Economics Co., Inc., Montvale, NJ, p. 1021, 1993.

(2) C. B. Fleet Co., "Phospho-Soda Complaints," January 8, 1987 to January 3, 1991, copy in OTC vol. 090TFM3, Docket No. 78N-036L, Dockets Management Branch.

(3) C. B. Fleet Co., "Product Complaint Record No. 6675," March 4, 1993, copy in OTC vol. 090TFM3.

(4) United States Pharmacopeia (USP), "Drug Problem Reporting Program No. 16921," March 31, 1993, copy in OTC vol. 090TFM3.

(5) C. B. Fleet Co., "Product Complaint Record No. 6337," July 21, 1992, copy in OTC vol. 090TFM3.

(6) C. B. Fleet Co., "Product Complaint Record No. 6753," April 21, 1993, copy in OTC vol. 090TFM3.

(7) McConnell, T. H., "Fatal Hypocalcemia from Phosphate Absorption from Laxative Preparation," *Journal of the American Medical Association*, 216:147–148, 1971.

(8) Wiberg, J. J., G. G. Turner, and F. Q. Nuttall, "Effect of Phosphate or Magnesium Cathartics on Serum Calcium," *Archives of Internal Medicine*, 138:1114–1116, 1978.

(9) Market Withdrawal Letter from L. A. Farrar, C. B. Fleet Co., to Distributors of Fleet Phospho-soda Products, dated May 6, 1993, included in OTC vol. 090TFM3.

IV. The Agency's Proposal for a Warning

The case reports clearly show that an overdose of sodium phosphate/sodium biphosphate solution can cause an electrolyte imbalance. This imbalance can cause severe reactions and result in death. Further, this imbalance could occur if an excess dose of either the oral solution or the rectal enema dosage form were used. To better protect consumers who use products containing these ingredients, the agency believes that the labeling should contain a warning alerting consumers not to exceed the recommended dose unless directed by a doctor. The agency is also including another sentence that alerts consumers that serious side effects may occur from excess dosage. Such information is currently included in the labeling of the oral dosage form of the major trade product containing sodium phosphate/sodium biphosphate solution (Ref. 1). Accordingly, the agency is proposing to add the following warning statements in § 334.58(c)(2) for products that contain phosphates identified in § 334.16(d), (e), or (f): "Do not exceed recommended dose unless directed by a doctor. Serious side effects may occur from excess dosage." Because of the dire consequences that can occur from an overdose of phosphates, the agency is proposing that these warning statements appear in boldface type as the first sentences under the heading warnings.

Reference

(1) Labeling for Fleet Phospho-soda, in OTC vol. 090TFM3, Docket No.78N–036L, Dockets Management Branch.

The agency has examined the economic consequences of this proposed rulemaking and has determined that it does not require either a regulatory impact analysis, as specified in Executive Order 12866, or a regulatory flexibility analysis as defined in the Regulatory Flexibility Act (Pub. L. 96–354). This rulemaking for OTC laxative drug products is not expected to have an impact on small businesses. The final rule will limit the OTC container size of one laxative drug product (sodium phosphate/sodium biphosphate oral solution) to 90 mL. This container size is currently allowed in the marketplace. Larger size containers will not be allowed. The manufacturer of the only major trade product marketed in a larger-size container has already withdrawn that size product from the market. The final rule will also require the addition of warning statements to product labeling. Manufacturers are encouraged to add these warning statements at the next label printing for affected products. Manufacturers will have a number of months until a final rule becomes effective to implement this labeling. The impact of a final rule appears to be minimal, therefore, the agency concludes that this proposed rule is not a major rule as defined in Executive Order 12866. Further, the agency certifies that this proposed rule will not have a significant economic impact on a substantial number of small entities as defined in the Regulatory Flexibility Act.

The agency invites public comment regarding any substantial or significant economic impact that this rulemaking would have on OTC laxative drug products. Comments regarding the impact of this rulemaking on OTC laxative drug products should be accompanied by appropriate documentation. The agency will evaluate any comments and supporting data that are received and will reassess the economic impact of this rulemaking in the preamble to the final rule.

The agency has determined under 21 CFR 25.24(c)(6) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

Interested persons may, on or before May 31, 1994, submit written comments on the proposed regulation to the Dockets Management Branch (address above). Written comments on the agency's economic impact determination may be submitted on or before May 31, 1994. Three copies of all comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document and may be accompanied by a supporting memorandum or brief. Received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

List of Subjects in 21 CFR Part 334

Labeling, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that

21 CFR part 334 (as proposed in the Federal Register of January 15, 1985 (50 FR 2124)) be amended as follows:

PART 334—LAXATIVE DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

1. The authority citation for 21 CFR part 334 continues to read as follows:

Authority: Secs. 201, 501, 502, 503, 505, 510, 701 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 321, 351, 352, 353, 355, 360, 371).

2. Section 334.16 is amended by revising the introductory text to read as follows:

§ 334.16 Saline laxative active ingredients.

The active ingredient of the product consists of any of the following when used within the dosage limits established for each ingredient in § 334.58(d) and when packaged according to § 334.25:

* * * * *

3. New § 334.25 is added to read as follows:

§ 334.25 Package size limitation.

Due to the toxicity associated with sodium phosphate/sodium biphosphate oral solution marketed in large size containers, any product containing sodium phosphate/sodium biphosphate oral solution shall not contain more than 90 milliliters per container.

4. Section 334.58 is amended by adding new paragraph (c)(2)(iv) to read as follows:

§ 334.58 Labeling of saline laxative drug products.

* * * * *

(c) * * *

(2) * * *

(iv) *Oral and rectal dosage forms.* "Do not exceed recommended dose unless directed by a doctor. Serious side effects may occur from excess dosage." [sentences in boldface type; sentences to appear as first statements under the heading "Warnings"]

* * * * *

Dated: March 22, 1994.

Michael R. Taylor,

Deputy Commissioner for Policy.

[FR Doc. 94–7630 Filed 3–30–94; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF THE INTERIOR

National Park Service

36 CFR Parts 5 and 7

RIN: 1024–AC15

Glacier National Park; Revision to Special Regulations

AGENCY: National Park Service, Interior.

ACTION: Proposed rule.

SUMMARY: The National Park Service (NPS) is proposing to revise its current regulations regarding sport fishing, the use of motorized vessels, and commercial passenger-carrying vehicles in Glacier National Park. First, the proposed rule would continue to allow fishing in most streams, rivers, and lakes in Glacier National Park, subject to closures or other conditions made by the Superintendent consistent with the park's fisheries program objectives. Second, the proposed rule would prohibit motorboat use on Kintla Lake, and place horsepower restrictions on other park lakes. Third, the proposed rule would clarify the exceptions to the prohibition regarding commercial passenger-carrying motor vehicles, and would expand the areas of the park in which these vehicles would be allowed.

DATES: Written comments will be accepted through May 31, 1994.

ADDRESSES: Comments should be addressed to: Superintendent, Glacier National Park, West Glacier, MT. 59936.

FOR FURTHER INFORMATION CONTACT: Fred Vanhorn, Protection Specialist, Glacier National Park, West Glacier, MT. 59936.

SUPPLEMENTARY INFORMATION:

Background

Fishing

The present Glacier National Park fishing regulations are codified in 36 CFR 7.3(a),(b), and (c). They permit fishing in selected waters of the park with a variety of regulations covering specific lakes and streams.

Technical fishery assistance has been provided to Glacier National Park by the U.S. Fish and Wildlife Service and its predecessors for 45 years. The present park management objectives have evolved since 1976 and are consistent with the park's primary purpose, which is to preserve natural environments and native plant and animal life, and to provide for the enjoyment of the resources by park visitors in ways that maintain natural conditions. The specific objectives of the park's fishery program are:

1. to manage the fishery as an integral part of the park's ecosystem;

2. to restore and preserve native species and aquatic habitats; and

3. to provide recreational fishing for the enjoyment of the park visitors when consistent with the two previous objectives.

Attainment of these objectives requires that angler harvests not alter native species natural replenishment rates or age structure, or significantly reduce numbers, biomass, or sizes from those occurring in un-fished populations. Protective policies of the NPS that have prevented significant degradation of the aquatic habitat have also restricted the use of maintenance stocking in park waters. Given these constraints, special angling regulations have become the primary means to accomplish park fishery objectives.

Regulations used to protect fish and maintain angling quality have included manipulating season dates, bait and terminal gear restrictions, and the use of creel limits, including catch and release. Additionally, various waters have been closed to anglers in order to protect threatened and endangered species, nesting birds, and visitors.

Because of the introduction of non-native fish in the past, the current invasion of non-native fish from outside the park, the recognition of the westslope cutthroat and bull trout as species of special concern by the State of Montana, and increased fishing in selected waters within the park, park management must be able to respond rapidly to changes that occur in a dynamic ecosystem resulting from human and natural conditions.

The proposed regulation would allow the Superintendent to meet these objectives in a timely manner by establishing a process to implement local Superintendent's orders using the discretionary authority of 36 CFR 1.5. Such orders could include restrictions or conditions on species of fish allowed for take, seasons and creel limits, methods of taking, or other conditions. This procedure will afford greater protection to the park's aquatic resources, be more responsive to public needs, and allow the park managers greater flexibility in responding to specific situations.

Public notice of conditions or restrictions established by the Superintendent would be provided through signs, maps, brochures, newspaper notices or other appropriate methods as required by 36 CFR 1.7. Detailed information pertaining to the nature and extent of fishing restrictions will be readily available to anglers in the park. Superintendent's restrictions and conditions on fishing will be reviewed at least annually and made a