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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 201

[Docket No. 78N-036L]

RIN 0910-AA01

Drug Labeling; Warning and Direction Statements for Rectal Sodium Phosphates for Over-the-Counter Laxative Use; Final Rule; Stay of Compliance

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule; stay of compliance.

SUMMARY: The Food and Drug Administration (FDA) is staying compliance for the regulation for warning and direction statements for over-the-counter (OTC) dibasic sodium phosphate/monobasic sodium phosphate (sodium phosphates) drug products intended for rectal (enema) use until December 7, 1998. The regulation established conditions under which the labeling must include warning and direction statements for oral and rectal sodium phosphates products. This stay of compliance applies only to rectal sodium phosphates products and is in response to requests and a citizen petition that the final rule did not allow sufficient time for relabeling of these products. This final rule is part of the ongoing review of OTC drug products conducted by FDA.

DATES: Section 201.307(b)(2)(ii) and (b)(3)(i) published on May 21, 1998 (63 FR 27836), are effective September 18, 1998, however, compliance with § 201.307(b)(2)(ii) and (b)(3)(i) as they relate to rectal sodium phosphates products is not mandatory until December 7, 1998.

FOR FURTHER INFORMATION CONTACT: Cheryl A. Turner, Center for Drug

Evaluation and Research (HFD-560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-2291.

SUPPLEMENTARY INFORMATION:

I. Background

In the **Federal Register** of March 31, 1994 (59 FR 15139), the agency proposed to amend the tentative final monograph for over-the-counter (OTC) laxative drug products to limit the OTC container size for sodium phosphates oral solution to not greater than 90 milliliters (mL). The agency also proposed a warning for all sodium phosphates products not to exceed the recommended dosage unless directed by a doctor.

In the **Federal Register** of May 21, 1998 (63 FR 27836), FDA issued a final rule for OTC laxative drug products containing sodium phosphates § 201.307(b)(1), (b)(2), and (b)(3) (21 CFR 201.307(b)(1), (b)(2), and (b)(3)) establishing a container size limitation of 90 mL for oral sodium phosphates (sodium phosphates oral solution), and new warning and direction statements for OTC oral and rectal sodium phosphates for relief of occasional constipation, or for preparing the colon for x-ray or endoscopic examination. On May 21, 1998 (63 FR 27886), FDA also issued a proposed rule to amend the tentative final monograph for OTC laxative drug products (21 CFR 334.16 and 334.58) to include additional general labeling and professional labeling for oral and rectal sodium phosphates and a new time-to-effect statement for rectal products.

The final rule requires manufacturers to add certain new labeling for rectal sodium phosphates drug products. The new warning in § 201.307(b)(2)(ii) states: "Using more than one enema in 24 hours can be harmful." The new directions in § 201.307(b)(3)(i) state: "Do not" ("take" or "use") "more unless directed by a doctor. See Warnings." The final rule specified an effective date of September 18, 1998, for these warning and direction statements for rectal sodium phosphates products.

In the final rule (63 FR 27836 at 27842), the agency stated that relabeling costs of the type required by this final rule generally average about \$2,000 to \$3,000 per stock keeping unit (SKU) (individual products, packages, and sizes). At that time, the agency was

aware of three manufacturers that together produce approximately 125 SKU's of rectal sodium phosphates drug products. The agency mentioned that there may be a few additional small manufacturers or a few additional products in the marketplace that are not identified in the sources FDA reviewed. The agency stated that some entities, especially those private label manufacturers that provide labeling for a number of the affected products, may incur significant impacts (63 FR 27836 at 27843).

In response to the final rule, the agency received two comments (Refs. 1 and 2) and two citizen petitions (Ref. 3). One private label manufacturer (Ref. 1) stated that the economic impact of the final rule was severe because it currently had 126 SKU's of rectal sodium phosphates products. The manufacturer stated that its relabeling cost was approximately \$3,500 per SKU or \$441,000. In addition, the cost of stickering the current inventory of 2 million printed folding cartons is \$160,000 with a capital expenditure of \$25,000. The cost of obsolescence for unused printed folding cartons during the transition period was estimated to be \$100,000, making total costs approximately \$776,000. The manufacturer requested that the implementation date of the final rule for enema products be 1 year after its effective date. A major manufacturer of oral and rectal sodium phosphates products (Ref. 2) objected to the content of the final rule and argued that the new warning and direction statements were not justified for rectal sodium phosphates products.

On July 15, 1998, at a public meeting between representatives of FDA and industry (Ref. 4), industry representatives stated the following concerns: (1) The warning in § 201.307(b)(2)(ii) would be confusing for consumers because it may conflict with how some physicians prescribe rectal sodium phosphates for cleansing the bowel in preparation for a medical procedure, and (2) 120 days is not enough time for manufacturers to relabel their rectal sodium phosphates products. Industry representatives suggested that the agency revise the warning to read: "Use only one enema in 24 hours unless recommended by a doctor. Serious side effects may occur from excess dosage." No revisions were

suggested for the direction statement in § 201.307(b)(3)(i).

Petitions (Ref. 3) for a "stay of action and reconsideration" for OTC enemas containing sodium phosphates, submitted in response to this meeting, requested: (1) An indefinite stay of the warning and directions required by § 201.307(b)(2)(ii) and (b)(3)(i), (2) revision of the warning in § 201.307(b)(2)(ii) to read: "Do not use more than one enema in a 24-hour period unless directed by a doctor," and (3) revision of the directions in § 201.307(b)(3)(i) to read: "Use only single daily dose unless directed by a doctor. See Warnings."

II. The Agency's Response

The agency acknowledged in its analysis of impacts in the final rule (63 FR 27836 at 27842) that private label manufacturers that provide labeling for a number of the affected products may incur significant impacts. Based on the comment's information (Ref. 1), the agency agrees that the economic impact for this specific manufacturer is high. In addition, other industry representatives concurred that 120 days was insufficient time for manufacturers to relabel their rectal sodium phosphates products. Therefore, the agency is staying compliance with the regulation for relabeling of rectal sodium phosphates products until December 7, 1998, to provide manufacturers additional time to comply with the labeling requirements of the final rule. Industry was previously informed of this stay of compliance with the regulation (Ref. 5). The agency is not granting a longer stay of compliance or an indefinite stay of compliance of this portion of the final rule because of the safety concerns discussed in the final rule (63 FR 27836 at 27840 to 27841).

The petitioner's request for reconsideration and revision of the warning and direction statements based on professional uses of these products is denied (Ref. 5). The warning in the March 31, 1994, proposed rule (59 FR 15139 at 15142) was intended to promote the safe, direct consumer use of these products. The agency considers the warning in § 201.307(b)(2)(ii) and the directions in § 201.307(b)(3)(i) in the May 21, 1998, final rule consistent with the safe, direct consumer use of rectal sodium phosphates products as intended in the proposed rule. The agency may reconsider the wording in this labeling if convincing data are submitted that demonstrate consumer

confusion. The agency believes that professional labeling for these products, which will be repropounded in a future issue of the **Federal Register**, will address any remaining labeling concerns.

Publication of this document constitutes final action on the warning and labeling directions for rectal sodium phosphates products in § 201.307(b)(2)(ii) and (b)(3)(i) under the Administrative Procedure Act (5 U.S.C. 553). Because this final rule is a stay of compliance of the regulation, FDA finds that the notice and comment procedures are unnecessary and not in the public interest (5 U.S.C. 553(b) and (d)). The agency believes that staying compliance with the regulation, as it relates to rectal sodium phosphates products, until December 7, 1998, will provide sufficient time for industry to implement the labeling revisions required for rectal sodium phosphates products.

III. References

The following references are on display in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, and may be seen by interested parties between 9 a.m. and 4 p.m., Monday through Friday.

1. Comment No. C190, Docket No. 78N-036L, Dockets Management Branch.
2. Comment No. LET176, Docket No. 78N-036L, Dockets Management Branch.
3. Comment No. PRC1, Docket No. 78N-036L, Dockets Management Branch.
4. Comment No. MM16, Docket No. 78N-036L, Dockets Management Branch.
5. Letter from D. Bowen, FDA, to P. Reichertz, Arent Fox Kintner Plotkin & Kahn, coded LET178, Docket No. 78N-036L, Dockets Management Branch.

IV. Analysis of Impacts

The economic impact of the final regulation was discussed in the final rule (63 FR 27836 at 27842 and 27843). A stay of compliance for the warning and direction statements for rectal sodium phosphates products will provide additional time for companies to relabel these products and will reduce label obsolescence, as there will be additional time to use up more existing labeling. Thus, this final rule granting a stay of compliance should reduce the economic impact on industry.

FDA has examined the impacts of the final rule (stay of compliance) under Executive Order 12866 and the

Regulatory Flexibility Act (5 U.S.C. 601-612). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency believes that this final rule is consistent with the regulatory philosophy and principles identified in the Executive Order. In addition, the final rule is not a significant regulatory action as defined by the Executive Order and so is not subject to review under the Executive Order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. This final rule provides a stay of compliance, which will provide manufacturers additional time to use up existing product labeling. Accordingly, the agency certifies that the final rule will not have a significant economic impact on a substantial number of small entities. Therefore, under the Regulatory Flexibility Act, no further analysis is required.

V. Paperwork Reduction Act of 1995

FDA concludes that the labeling requirements in this document are not subject to review by the Office of Management and Budget because they do not constitute a "collection of information" under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*). Rather, the labeling is a "public disclosure of information originally supplied by the Federal Government to the recipient for the purpose of disclosure to the public" (5 CFR 1320.3(c)(2)).

VI. Environmental Impact

The agency has determined under 21 CFR 25.31(c) 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.

Dated: December 1, 1998.

William K. Hubbard,

*Associate Commissioner for Policy
Coordination.*

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