DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

AUG 6 2001

Peter S. Reichertz, Esq.
Arent, Fox, Kintner, Plotkin & Kahn
1050 Connecticut Avenue, NW
Washington, D.C. 20036-5339

Re: Docket No. 78N-036L/CP21

Dear Mr. Reichertz:

This letter responds to a citizen petition (CP21) submitted on behalf of the C. B. Fleet Company, Inc., dated June 9, 1995, under Docket No. 78N-036L in FDA's Dockets Management Branch. The petition requested that FDA amend the tentative final monograph (TFM) for over-the-counter (OTC) laxative drug products (published in the Federal Register of January 15, 1985, 50 FR 2124) to allow: (1) A dosage range of 17 to 25 grams (g) for magnesium citrate in a powder for reconstitution as an oral solution when used in a bowel cleansing kit; (2) use of bisacodyl in an enema dosage form as an alternative to bisacodyl suppositories in bowel cleansing systems; and (3) greater flexibility in timing of administration of the components of bowel cleansing systems. The petition included journal articles and information from several textbooks in support of the requests.

The agency has reviewed the submitted data and other relevant information and has determined that use of the rectal enema dosage form of bisacodyl for laxative use and as part of a bowel cleansing system is as effective as the suppository form of bisacodyl as previously stated (see letter from W. Gilbertson, FDA, to you, dated October 26, 1989 (coded LET40)). We note that bisacodyl enema is the subject of a United States Pharmacopeial monograph. Accordingly, the agency intends to include bisacodyl in an enema dosage form as an alternative to bisacodyl suppositories in bowel cleansing systems in the OTC laxative final monograph.

We have also concluded that the submitted data are inadequate to support your requests to amend the TFM for OTC laxative drug products to include a dosage range of 17 to 25 g magnesium citrate in a powder for reconstitution in a bowel cleansing kit and to provide greater flexibility in timing of administration of the components of bowel cleansing systems. We have the following specific comments.

In the TFM, the proposed dose for bowel cleansing systems containing magnesium citrate is 25 g in oral solution (50 FR 2156 and 2157). The agency based the dosage and directions for the bowel cleansing systems in proposed §§ 334.66(d)(3)(iii)(a) and (d)(3)(iii)(b) on data

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submitted in response to the TFM. The agency has rereviewed the data and determined that an error was made in the dosage. The data showed that 296 to 340 mL (17.2 to 24.1 g) of magnesium citrate oral solution, USP was used. Magnesium citrate oral solution, USP contains 5.8 to 7.1 g of magnesium citrate per 100 mL, which equates to a dosage of 17.2 to 24.1 g in the studies. Therefore, in the OTC laxative final monograph, the agency will change the dosage for magnesium citrate in oral solution from 25 g (350 mL) to a range of 17.2 to 24.1 g (296 to 340 mL).

However, before a dose of 17.2 to 24.1 g magnesium citrate in a powder for reconstitution can be included in the OTC laxative final monograph, specific labeling information needs to be provided. Labeling for magnesium citrate powder must include any warnings and directions specific to use of the powder, particularly detailed instructions for reconstituting the magnesium citrate powder when taken in a single or divided dose as proposed in § 334.58(d)(2) or when used in a bowel cleansing system. Further, if magnesium citrate in a powdered dosage is included in the monograph for OTC laxative drug products, the agency will limit marketing to premeasured packets only, to avoid dosing errors.

The studies included in the petition do not provide sufficient data to support your request for flexible timing intervals for administration of the components of bowel cleansing systems. The agency needs further clarification of the meaning of "flexibility in timing." For example, the sponsor proposes to amend the directions in proposed §§ 334.66(d)(3)(iii)(a) and (d)(3)(iii)(b) with such qualifications as "at least 2 hours," "at least 9 hours," and "approximately 2 hours." We believe that the ambiguity of these suggested timing intervals will not increase consumers' understanding of the appropriate times to administer the various components of a bowel cleansing system. We consider the current proposed specific timing intervals as set forth in §§ 334.66(d)(3)(iii)(a) and (d)(3)(iii)(b) of the TFM as providing meaningful and adequate directions to ensure the maximum effectiveness of these bowel cleansing kits.

We recommend that your client submit studies that compare the effectiveness of its proposed bowel cleansing kits to the bowel cleansing kits currently proposed in the TFM. These studies should include (1) all of the requested bowel cleansing components (but the dose of magnesium citrate should be between 17.2 and 24.1 g, as discussed above) and (2) your proposed time intervals for administration. This information can then be used to determine if varying the timing of administration influences the ability to perform an excellent quality barium enema or endoscopic procedure. We also recommend that the protocols for such comparative studies be sent to us for review prior to initiation of any studies.

In conclusion, the agency has determined that a bisacodyl enema dosage form may be used as an alternative to bisacodyl suppositories and that a dosage range of 17.2 to 24.1 g magnesium citrate in oral solution is also acceptable. Magnesium citrate 17.2 to 24.1 g in a powder for reconstitution as an oral solution could be included in a future amendment to the laxative final

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 8.9.01

FROM: Director
Division of OTC Drug Products, HFD-560

SUBJECT: Material for Docket No. 78N-036L

TO: Dockets Management Branch, HFA-305

[X] The attached material should be placed on public display under the above referenced Docket No.

[X] This material should be cross-referenced to Comment No. CP21

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Charles J. Ganley, M.D.

Attachment