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May 6, 2004

VIA FEDERAL EXPRESS

Division of Dockets Management  
(HFA-305)  
Food and Drug Administration  
5630 Fishers Lane, Room 1061  
Rockville, Maryland 20852

Re: Laxative Drug Products for Over-the Counter Human Use; Reopening of the  
Administrative Record  
**DOCKET 1978N-036L**

Dear Sir/Madam:

We represent C.B. Fleet Company, Incorporated, of Lynchburg, Virginia 24502 ("Fleet"). Fleet is the manufacturer and distributor of a number of Over-the-Counter ("OTC") laxative drug products for human use, including Fleet® Enemas (both Sodium Phosphates and Mineral Oil), Fleet® Phospho-soda® (Sodium Phosphates Oral Solution, USP), Fleet® Glycerin Suppositories, Fleet® Bisacodyl laxatives (enema, suppositories, and tablets) and Fleet® bowel preparation kits. On behalf of Fleet, we submitted, on January 19, 2004, additional data in response to the reopening of the administrative record on OTC Laxative Drug Products for Human Use, in response to the notice dated October 22, 2003, at 68 Fed. Reg. 60302 ("the Notice").

In comment 5, pages 9-11, of those comments, Fleet requested that the dose of Sodium Phosphates Oral Solution, USP, should be limited to 10-20 mL per dose when used as a laxative

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for relief of occasional constipation. In those comments, Fleet indicated that in its 1973 submission of data to the rulemaking on laxative drug products, it had stated that 4 teaspoonfuls (20 mL) was the most effective laxative dose, and that its Fleet® Phospho-soda® product had been so labeled for years prior to that time with a 2 teaspoon to 4 teaspoon laxative dose. Fleet further indicated it could not explain, based on its own records or those in the laxative rulemaking docket, why the dose had been set at 4 to 9 teaspoonfuls (20-45 mL).

As indicated therein, while Fleet believes that dosages above 20 mL are safe and effective, Fleet believes that above 20 mL the product has more of a purgative effect appropriate for bowel cleansing prior to medical procedures, but inappropriate for relief of occasional constipation. The product at dosages above 20 mL certainly relieves constipation, and is effective and appropriate for bowel cleansing, but Fleet believes such dosage is not appropriate for strictly laxative use.

As further support for the fact that a 10 mL to 20 mL dose is safe and effective for laxative use, enclosed please find enclosed as Exhibit A a press release issued by InKine Pharmaceuticals, Inc., on a study of VISICOL® tablets. (Each VISICOL® tablet contains the equivalent of 2.27 mL of Sodium Phosphates Oral Solution.) This was a study of forty patients with chronic constipation. Patients received either four tablets or eight tablets, given in two-four tablet dosages. (This would, therefore, be equivalent to about 9.08 mL or 18.16 mL of Fleet® Phospho-soda®). Both doses were found to be safe and effective in treatment of chronic constipation, with no withdrawals due to serious adverse events. (There were four withdrawals

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due to non-serious adverse events in the 8 tablet arm). In the four tablet arm of the study, there were no significant changes in electrolyte levels after four weeks of therapy, and in the 8 tablet arm, only a modest, but statistically significant, decrease in serum potassium. The eight tablet dose produced more bowel movements (10) in the first week as compared to the four tablet dose (7), but the differences were not statistically significant after the first week.

While this study is of a different product for a different indication, the product and the dose given are similar to the 10-20 mL dose recommended by Fleet for inclusion in the Final Monograph on Laxative Drug Products for Over-the-Counter Human Use, ("Final Monograph"), as is the indication (occasional vs. chronic constipation). These results provide further evidence that 10-20 mL dosing of Sodium Phosphates Oral Solution, USP, is the proper OTC laxative dose. The results also show that the equivalent of the 20 mL dose is more effective in the first week; Fleet® Phospho-soda® is only indicated for use of occasional constipation for one week. There is thus support for the dose range proposed by Fleet.

In addition, please find enclosed as Exhibit B an abstract of a study called "Safety and Laxative Effects of VISICOL® Tablets (Sodium Phosphate) in Healthy Volunteers", by Rose et al. This was a study in 31 patients comparing 8 to 12 tablets of VISICOL® to 17g of polyethylene lavage (PEG) (MIRALAX®). Both the 8 and 12 tablet dosages of VISICOL® (Sodium Phosphates) Tablets produced more bowel movements than the NDA approved MIRALAX® (PEG) laxative product. Both change in stool consistency and time to effect were better in the VISICOL® treated subjects. Indeed, dose reductions were necessary in the

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VISICOL® group. There were no significant side effects in the VISICOL® group, and changes in electrolytes did not differ significantly following completion of dosing.

This study is further evidence that a 20 mL dose of FLEET® Phospho-soda® (equivalent to 8 VISICOL® tablets) is an effective dose, and the results suggest it may be the most effective dose.

\* \* \* \* \*

For the above reasons, Fleet again requests that the laxative dose of Sodium Phosphates Oral Solution, USP, be limited to 10-20 mL, when the Final Monograph is published. Fleet will submit further data on this study (and any other relevant information) as it becomes available.

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**CERTIFICATION**

The undersigned certifies that, to the best knowledge and belief of the undersigned, this submission includes all information and views on which this submission relies, and includes representative data and information known to the submitter which are unfavorable to the submission.

Respectfully Submitted

SONNENSCHN NATH & ROSENTHAL LLP

By:



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Counsel for C.B. Fleet Company, Incorporated