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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUL 23 1991

Peter S. Reichertz, Esquire
Arent Fox Kinter Plotkin & Kahn
1050 Connecticut Avenue, N.W.
Washington, D.C. 20036-5339

Re: Docket No. 78N-036L
Comment No. CP10

Dear Mr. Reichertz:

This is in response to your citizen petition dated April 22, 1991, submitted on behalf of C. B. Fleet Co., Inc., and filed in FDA's Dockets Management Branch as CP10 under Docket No. 78N-036L. The petition requests amendment of the tentative final monograph for over-the-counter (OTC) laxative drug products to list separately the response times for the different forms of rectally administered stimulant laxatives (i.e., suppositories and enemas) so as to include a different response time (5 to 20 minutes) for enemas.

In your petition, you state that the tentative final monograph on OTC laxative drug products presently does not distinguish the response times for the different forms of rectally administered stimulant laxatives. You mention that the response time for rectal dosage forms is listed in proposed § 334.60(b)(2) as 1/4 to 1 hour, based only on a review of suppositories. You add that a response time for an enema dosage form of stimulant laxatives is needed because the agency plans to add this dosage form to the monograph as discussed in my October 26, 1989 letter (coded LET40 under the same docket) to you responding to a citizen petition (coded CP7) filed by Fleet.

You state in the petition that enemas, because of the introduction of a liquid, work faster than suppositories, which must melt. In addition, enemas introduce a greater volume of liquid which also has an osmotic volume laxative effect. You cite two unpublished studies (a 1978 study by Salen and Keating, "A Comparative Study of Four Laxative Products", and a study by B. B. Swerdlow, "An Evaluation of a Bisacodyl Small Volume Enema") as supporting evidence that the mean response time for the bisacodyl enema is from 5 to 20 minutes, not 15 minutes to 1 hour. Accordingly, you requested amendment of the tentative final monograph for OTC laxative drug products to include a response time of 5 to 20 minutes for stimulant laxative enemas and that this information be included in the final monograph on OTC laxative drug products when published.

As noted in my letter of October 26, 1989, I informed you that we had determined that a 10-milligram (mg) dose of bisacodyl, administered in a 37.5 milliliter (ml) aqueous suspension rectal enema formulation, is safe and effective for use by adults and children 12 years of age and over. Based on the study by Salen and Keating, comparing two dosages of a bisacodyl enema with a bisacodyl suppository and a bisacodyl microenema, the agency determined that only the criterion "time to response" provides information suggesting that the bisacodyl products can be differentiated from one another. Based on the 59-percent patient response rate within 15 minutes for the bisacodyl enema and the 32-percent patient response rate within 15 minutes for the bisacodyl suppository control group, the agency found that the study, although qualitative and not optimally designed, provided substantial evidence that the enema containing 10 mg bisacodyl in a 37.5 ml aqueous suspension is at least as effective as the 10 mg bisacodyl suppository.

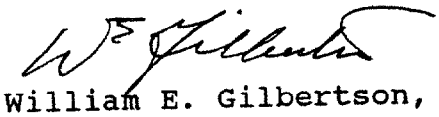
The study by Swerdlow showed a 90-percent response rate with a mean time of 10 minutes to first response after the administration of the bisacodyl enema. The agency determined that, although this study was uncontrolled, its favorable results are of value primarily as support for the results of the Salen and Keating study.

Based on these studies, the response time that you suggest appear to be reasonable. Based on the earlier petition (CP7) that we reviewed and information already included in the administrative record for the rulemaking for OTC laxative drug products, the agency already plans to address the issue of response time for a stimulant laxative enema in the final monograph for OTC laxative drug products. Therefore, we do not plan to propose such a response time in an amendment to the tentative final monograph. Your petition will remain part of the public record for this rulemaking and, as you have requested, the issue of response time will be addressed in the final monograph.

Any comment you may wish to make on the above information or any additional information that you may wish to provide should be submitted in triplicate, identified with the docket and comment numbers shown at the beginning of this letter, to the Dockets Management Branch (HFA-305), Food and Drug Administration, Room 1-23, 12420 Parklawn Drive, Rockville, MD 20857.

We hope this information will be helpful.

Sincerely yours,



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