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R. William Soller, Ph.D.
Senior Vice President and
Director of Science & Technology
Consumer HealthCare Products Association
1150 Connecticut Avenue, N.W.
Washington, D.C. 20036-4193

RE: Docket No. 81N-0033
LET 053

Dear Dr. Soller:

This letter responds to your letter dated June 21, 2002 regarding the research program on benzocaine for toothache. You provided the following information:

- A retrospective analysis of previously submitted studies to support a dose response for benzocaine 10% and 20%;
- A proposal to conduct a pilot study to demonstrate that study subjects with toothache understand the proposed directions for use in the clinical efficacy study;
- A proposal to conduct an efficacy study evaluating 20% benzocaine.

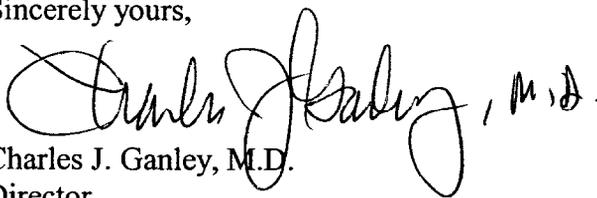
The Division of OTC Drug Products, in cooperation with the Division of Dermatologic and Dental Drug Products, has the following comments.

1. The retrospective analysis conducted by William Thompson, Ph.D. does not adequately support the dose response of benzocaine. In our letter dated July 17, 1998, the Division of OTC Drug Products noted numerous deficiencies in the conduct of the studies. These deficiencies still exist. A reanalysis of these studies using efficacy criteria agreed upon for a future study does not adequately support the dose response.
2. The pilot study appears to be a logical mechanism to determine whether subjects will be able to use the product.
3. The proposed clinical efficacy study should include treatment arms of 10% and 20% benzocaine, since both products are to be marketed. Each product would be required to be superior to a placebo and a dose response must clearly be established.

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4. A study in which the benzocaine products are administered only once, rather than repeatedly will be acceptable. The timing of subsequent doses in labeling can be based on evaluation of the duration of effect data obtained from the proposed clinical efficacy study. Without having empirical data to support the effectiveness of subsequent doses, the labeling of these products will need to include language that directs the consumer to seek immediate treatment from a dentist if significant relief is not obtained after several doses. The labeling should also be clear that the product is for temporary relief of toothache so that the consumer can make arrangements to obtain definitive dental care.
5. In our July 17, 1998 letter, the Division stated that an additional single study was needed to support the efficacy data for benzocaine already submitted to the Agency. Both Divisions agree that only one additional successful efficacy study would suffice if it evaluates both 10% and 20% benzocaine. We strongly recommend that the protocol be submitted to the agency for review before commencing the study.
6. In our January 8, 2002 letter, the Division raised concerns about the risk of methemoglobinemia associated with benzocaine. We would like an updated assessment of the reports of methemoglobinemia associated with the use of benzocaine products for this condition of use. These cases should be obtained from representative companies in your organization who market these products and who have not already reported the cases to the agency. You should also undertake a review of the medical literature. Your assessment should include a description of the types of cases and include demographic, dosing and outcome information. You should also propose how this adverse event should be addressed in the labeling of these products.

Sincerely yours,



Charles J. Ganley, M.D.

Director

Division of OTC Drug Products

Office of Drug Evaluation V

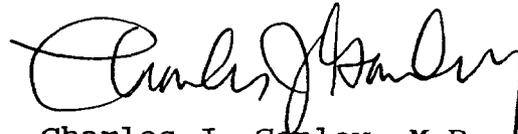
Center for Drug Evaluation and Research

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: 10/30/02
FROM: Director
Division of OTC Drug Products, HFD-560
SUBJECT: Material for Docket No. 81N-0033
TO: Dockets Management Branch, HFA-305

- The attached material should be placed on public display under the above referenced Docket No.
- This material should be cross-referenced to Comment No. LET 053


Charles J. Ganley, M.D.

Attachment