

ADMINISTRATIVE STAFF

Food and Drug Administration  
Rockville MD 20857

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APR 15 1982

•George F. Hoffnagle, Sc. D.  
Vice President for Scientific and  
Regulatory Affairs  
Vick Divisions Research and  
Development  
Richardson-Vicks Inc.  
One Bradford Road  
Mount Vernon, NY 10553

Re: Docket No. 76N-052N  
Comment No. C0111  
Comment No. CR003  
Comment No. SUP15

Dear Dr. Hoffnagle:

This letter concerns the data on the effectiveness of the combination of l-desoxyephedrine and aromatics (camphor, menthol, methyl salicylate, bornyl acetate, and lavender oil) as a topical nasal decongestant (administered by inhaler), that were submitted by your company on October 10, 1972 (initial submission), March 15, 1979, and June 3 and December 6, 1980, in relation to the advance notice of proposed rulemaking on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products which was published in the FEDERAL REGISTER on September 9, 1976. Based on these data, Vicks requested that l-desoxyephedrine, alone and in combination with aromatics (camphor, menthol, methyl salicylate, bornyl acetate, and lavender oil), be classified in Category I.

The Bureau of Drugs notified you in a letter dated May 4, 1981, that studies 74-10A, 74-30, 74-58, 75-45, and 70-24, as well as additional data in your submissions, provided sufficient evidence to classify l-desoxyephedrine (alone) in Category I as a topical nasal decongestant (in an inhaler).

The Bureau has determined that four of these studies also support the Category I classification of the combination of l-desoxyephedrine and aromatics. In study 74-30, statistical analysis of nasal air flow rates showed significant decongestion of the nostrils treated with the combination of l-desoxyephedrine and aromatics when compared to placebo. In study 74-58, statistical analysis of nasal air flow rates showed significant decongestion of the nostrils treated with the l-desoxyephedrine and aromatics combination when compared to the aromatics alone or the placebo at 5, 20, and 40 minutes after treatment. In study 70-24, statistical analysis of nasal air flow rates showed significant decongestion of the nostrils treated with the combination of l-desoxyephedrine and aromatics

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when compared to the placebo and to 1-desoxyephedrine alone. The Bureau's evaluation of these studies is contained in my May 4, 1981 letter.

The studies indicate that the aromatic mixture has an adjuvant type effect when combined with 1-desoxyephedrine, i.e., although the aromatic mixture when tested alone has little effect, the effectiveness of 1-desoxyephedrine is enhanced when combined with the aromatic mixture.

Paragraph 5 of the agency's "General Guidelines for OTC Drug Combination Products, September 1978" (a notice of the availability of these guidelines was published in the FEDERAL REGISTER of November 28, 1978 (43 FR 55466)) provides that "in some cases an ingredient may be appropriate for use only in a specific combination or data may be available only to support the use of the ingredient in combination but not as a single ingredient. In such cases the ingredient will be placed in Category I for use only in permissible combinations and not as a single ingredient."

Based on the above guidelines and the data reviewed, the Bureau is classifying the 150 mg aromatic mixture alone (i.e., camphor (54 mg), menthol (80 mg), methyl salicylate (11 mg), bornyl acetate (0.2 mg), and lavender oil (4 mg)), as Category II; and the 150 mg aromatic mixture in combination with 50 mg of 1-desoxyephedrine is classified as a Category I topical nasal decongestant to be administered by a nasal inhaler. The proposed adult dosage of the combination is two inhalations in each nostril not more often than every 2 hours from an inhaler that delivers in each 800 mL of air 0.04 to 0.15 mg of 1-desoxyephedrine. In keeping with the guidelines established by the Panel (41 FR 38333), the dosage for children 6 to under 12 years of age is one-half of the adult dosage. Because neither 1-desoxyephedrine nor the aromatic mixture caused rebound nasal congestion when inhaled every 2 hours six times daily for a 7-day period, the use of the combination of 1-desoxyephedrine and aromatics will be limited to not more than 7 days rather than the 3-day limit that the Panel recommended for other topical nasal decongestants that cause rebound congestion.

The Bureau intends to recommend to the Commissioner that the agency respond to these data in the above manner in the tentative final monograph for OTC nasal decongestant drug products which will be published in a future issue of the FEDERAL REGISTER. Following that publication, you will have

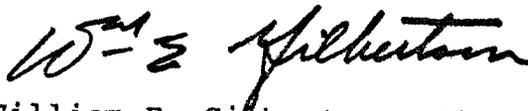
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the opportunity to object to the agency's conclusions or to submit additional data. In the interim we would be glad to discuss these data in more detail if you feel it is necessary.

We hope this information will be helpful.

Sincerely yours,

A handwritten signature in cursive script that reads "W. E. Gilbertson". The signature is written in dark ink and is positioned above the typed name.

William E. Gilbertson, Pharm. D.  
Director  
Division of OTC Drug Evaluation  
Bureau of Drugs

# MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION

TO : Dockets Management Branch (HFA-305)

DATE: APR 15 1982

FROM : Director  
Division of OTC Drug Evaluation (HFD-510)

SUBJECT: Material for Docket No. 76N-052N

- The attached correspondence should be placed on public display under the above referenced Docket No.
- This correspondence should be cross-referenced to Comment CO111, CR003, and SUP 15.



William E. Gilbertson, Pharm. D.

Attachment