



JUN 8 1982

Edward J. Hiross, Ph. D.  
Drug Regulatory Affairs  
Sterling Drug, Inc.  
90 Park Avenue, 8th floor  
New York, NY 10016

RE: Docket No. 76N-0052  
Comment No. C0125

Dear Dr. Hiross:

This letter is in response to the December 8, 1976 letter and submission from Dr. B. G. Crouch, Director, Drug Regulatory Affairs, Sterling Drug Inc., to the Hearing Clerk of the Food and Drug Administration (FDA) regarding Neo-Synephrine 1% Nose Drops. Dr. Crouch's letter pertains to the report and proposed monograph of the Advisory Review Panel on OTC Cold, Cough, Allergy, Bronchodilator, and Antiasthmatic Drug Products which was published in the FEDERAL REGISTER on September 9, 1976.

In the letter, Dr. Crouch stated that, although a submission on Neo-Synephrine 1% was made to the Panel on October 10, 1972, the Panel did not categorize the 1-percent concentration of phenylephrine hydrochloride. Dr. Crouch requested that Neo-Synephrine 1% be categorized as a Category I OTC topical nasal decongestant.

The Bureau of Drugs has reviewed the two studies submitted to support your company's request to place 1 percent phenylephrine hydrochloride in Category I for OTC use as a topical nasal decongestant. The first study demonstrated that 1 percent and 0.5 percent phenylephrine hydrochloride are both effective as nasal decongestants based on a subjective grading of edema and erythema to evaluate nasal congestion. Nasal irritation occurred with both concentrations. Statistical analysis showed no significant difference between the two concentrations with respect to effectiveness.

The second study also demonstrated that 0.5 and 1 percent concentrations were effective nasal decongestants. The study was double-blind, and the evaluation of nasal congestion was based on both objective and subjective criteria. Statistical analysis of the results indicated that both solutions were effective decongestants ( $p < 0.001$ ). Twelve subjects who received the 1-percent concentration and 10 who received the 0.5-percent concentration experienced side effects such as headache, nausea, dizziness, nasal edema, and erythema. The differences in side effects between the two groups were not statistically significant. However, the data did suggest that the 1-percent concentration seemed more likely to induce

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# MEMORANDUM

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

TO : Dockets Management Branch (HFA-305)

DATE: JUN 9 1962

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

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



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



This material should be cross-referenced to Comment C0125.



William E. Gilbertson, Pharm. D.

Attachment

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U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE

rebound congestion. The investigator also noted that the 0.5-percent concentration may be slightly better tolerated.

After reviewing these data, the Bureau concludes that 1 percent phenylephrine hydrochloride is a safe and effective topical nasal decongestant for OTC use. The Bureau, therefore, proposes to place 1 percent phenylephrine hydrochloride as a topical nasal decongestant in Category I. The Bureau proposes that a 1-percent aqueous solution of phenylephrine hydrochloride be labeled for adult use only at a dosage of 2 or 3 drops or sprays in each nostril not more often than every 4 hours. The warnings recommended by the Panel for topical nasal decongestants in § 341.80(b)(1) (41 FR 38423) are also applicable to the 1-percent concentration of phenylephrine hydrochloride. Additionally, because of a possible rebound effect with continued use of the 1-percent solution, the Bureau proposes the following warning for the 1-percent concentration of phenylephrine hydrochloride: "Frequent use of this product may cause nasal congestion to recur or worsen."

The Bureau intends to recommend to the Commissioner that the agency respond to your company's data in the above manner in the tentative final monograph for nasal decongestant drug products, which will be published in a future issue of the FEDERAL REGISTER. Following that publication, you will have the opportunity to object to the agency's conclusion or to submit new data in support of your request.

We hope this information will be helpful.

Sincerely yours,



William E. Gilbertson, Pharm. D.  
Director  
Division of OTC Drug Evaluation  
Office of Drugs  
Bureaus of Drugs and Biologics