DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUN - 4 1998

**TRANSMITTED VIA FACSIMILE**

George R. Hemsworth, Ph.D.
Director, Regulatory Affairs
Carter-Wallace, Inc.
Half Acre Road
P.O. Box 1001
Cranbury, NJ 08512-0181

**Re: NDA# 20-114**
Astelin (azelastine HCL) Nasal Spray
MACMIS ID# 6611

Dear Dr. Hemsworth:

This letter concerns Carter-Wallace, Inc.'s (Wallace's) promotional materials and activities for the marketing of Astelin (azelastine HCl) Nasal Spray reviewed by the Division of Drug Marketing, Advertising, and Communications (DDMAC) as part of its monitoring program. DDMAC has reviewed these materials and concluded that CW is disseminating promotional materials for Astelin[1] that contain statements, suggestions, or implications that are false, lacking in fair balance or otherwise misleading in violation of the Federal Food, Drug, and Cosmetic Act and implementing regulations. Furthermore, it appears that these promotional materials were not submitted as required by 21 CFR 314.81(b)(3)(i).

The teleconference guidebook and poster materials claim superiority (by graph and text) of Astelin over Rhinocort (budesonide) Nasal Spray compared to baseline for the following efficacy parameters at ($P<0.05$):

- significantly decreased nasal congestion scores
- significantly decreased nasal airway resistance
- significantly increased nasal inspiration peak flow

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1 These promotional materials include, but are not limited to, an exhibit booth poster "Effect of azelastine on congestion in a study with budesonide" at the AAAAI conference in Washington, D.C., on March 12-17, 1998; and a teleconference guidebook "Discussion of Antihistaminic/Anti-inflammatory Activity of Azelastine HCl" sponsored and controlled by Wallace.

- significantly reduced total nasal symptom scores
- significantly reduced the number of sneezes after a nasal allergen challenge
- significantly reduced rhinorrhea

These materials are violative because they make statements, suggestion, or implications that Astelin is superior to Rhinocort, when such has not been demonstrated by substantial evidence (i.e., adequate and well-controlled studies). The cited reference[2], a small (n=14) open-label study is inadequate in scope and design to substantiate the superiority claims. Furthermore, this presentation lacks fair balance concerning safety risk information.

The teleconference handbook also includes a misleading comparative graphical presentation of Astelin, beclomethasone, and placebo. The presentation suggests or implies that Astelin is superior to beclomethasone because only positive Astelin results are displayed, based on "cherry-picked" secondary, non-validated endpoint data (visual analogue symptom scores). However, the results for the validated primary endpoint (total symptom scores, measured on a four-point scale) that demonstrated beclomethasone provided greater improvement than both Astelin and placebo are not disclosed. In addition, this presentation lacks fair balance concerning safety risk information or whether these are non-U.S. formulations of these products.

Therefore, Wallace should immediately cease its use of promotional materials and activities that contain these or similar claims of Astelin's superior efficacy. Wallace's written response should be received by DDMAC no later than June 18, 1998, describing the corrective steps that the Company has taken to ensure that the use of these materials have been suspended. Please direct your response to the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm 17-B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds CW that only written communications are considered official.

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[2] Wang, et al., "Effect of topical applications of budesonide and azelastine on nasal symptoms, eosinophil count, and mediator release in atopic patients after nasal allergen challenge during the pollen season." Intl Arch Allergy Immunol. 1997;114:185-192.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #6611 in addition to the NDA number.

Sincerely,

Joan Hankin, ~~JD~~
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications