DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FOI

JUN 24 1998

TRANSMITTED VIA FACSIMILE

Ms. Mary Jane Nehring
Director, Marketed Products Support
Worldwide Regulatory Affairs
Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

RE: **NDA#** 20-762
Nasonex (mometasone furoate monohydrate) Nasal Spray, 50 mcg
MACMIS# 6641

Dear Ms. Nehring:

This letter concerns Schering Corporation's (Schering) promotional materials and activities for the marketing of Nasonex (mometasone furoate monohydrate) Nasal Spray. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed these materials as part of its monitoring program and has concluded that Schering is disseminating Nasonex promotional materials that contain statements, suggestions, or implications of clinical superiority that are false or misleading in violation of the Federal Food, Drug, and Cosmetic Act and implementing regulations.

- Misleading Claims That Nasonex Is Superior To Flonase

Schering is promoting the superiority of Nasonex over Flonase (fluticasone propionate) (FP) through use of misleading promotional materials (e.g., detail aid NX0133 and the Mandl reprint). The Nasonex detail aid claims superiority of Nasonex compared to FP by selectively presenting (i.e., "cherry-picking") certain secondary efficacy endpoint data that misleadingly suggest that Nasonex demonstrated overall superiority over FP for the treatment of perennial allergic rhinitis (PAR) (i.e., for patient or physician evaluation of overall condition of PAR, Nasonex was more effective than FP at week 12 and endpoint, and at week 8, week 12, and endpoint, respectively). In written launch comments on November 3, 1997, DDMAC objected to these misleading cherry-picked presentations. In additional launch comments on other comparative Nasonex claims (letters dated December 16, 1998 and January 9, 1998), DDMAC reminded Schering that comparative clinical efficacy data between Nasonex and FP submitted to NDA# 20-762 do not support a clinical superiority claim for Nasonex.

These Nasonex superiority claims are based on a study by Mandl, et al. ("Comparison of once daily mometasone furoate and fluticasone propionate aqueous nasal sprays for the treatment of allergic rhinitis", Annals of Allergy, Asthma, & Immunology, 79: 370-378, 1997). Schering is distributing this study article reprint to support its Nasonex superiority claim over Flonase. However, various results of efficacy variables reported in the Mandl reprint contradict Schering's Nasonex overall superiority claim. In particular, Nasonex was not statistically different from FP at any time period for the primary efficacy variable (patient rated mean AM plus PM total nasal symptom score changes from baseline, averaged over 15-day intervals and at endpoint and week off treatment). Therefore, because Nasonex did not achieve statistical significance at the primary endpoint, the Nasonex superiority claims are unsubstantiated and the selective presentation of secondary efficacy data at certain timepoints showing statistical significance is misleading.

- Comparative Pharmacology Data Misleadingly Imply Nasonex Clinical Superiority

In Nasonex detail aids (NX0130 and NX0104), Schering presents a chart of six nasal corticosteroid products that compare *in vitro* pharmacology data about inhibition of mediator release ("Nasonex inhibits mediators of inflammation, such as IL-4, IL-5" and comparative chart, "lower scores (lowest for Nasonex) indicate more potent inhibition of mediators"). The comparative pharmacology chart and claims misleadingly suggest or imply clinical superiority of Nasonex over the other listed drugs in treating allergic rhinitis based on *in vitro* data from cell cultures from normal donors, when no such clinical significance has been demonstrated by substantial evidence (adequate and well-controlled head-to-head clinical trials). Furthermore, the disclaimer "The clinical relevance of these data in the treatment of allergic rhinitis is not known" does not remedy the misleading representation that Nasonex is clinically superior to the other corticosteroids. DDMAC addressed the overall concept of implied clinical superiority claims based on comparative pharmacology data with various Nasonex launch proposals, culminating with final DDMAC comments on January 9, 1998 that objected to several proposed comparative pharmacology claims as misleading unsubstantiated superiority claims. DDMAC's comments are applicable to the above implied clinical superiority claim (based on relative inhibition of mediator release) as well as to any other comparative *in vitro* and *in vivo* claims that have not been demonstrated by substantial evidence.

Schering should immediately cease its use of promotional materials and activities that contain these or similar claims of superiority for Nasonex. Schering's written response should be received by DDMAC no later than July 9, 1998, describing the corrective steps that the company has taken to ensure that the use of these materials has 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 Schering that only written communications are considered official.

In all future correspondence, regarding this particular matter, please refer to MACMIS ID # 6641 in addition to the NDA number.

Sincerely,

/S/

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