DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FOI

Food and Drug Administration
Rockville MD 20857

APR 8 1998

TRANSMITTED VIA FACSIMILE

Ms. Barbara A. Thompson
Assistant Director, Advertising Policy
Regulatory Affairs
Glaxo Wellcome Inc.
5 Moore Drive
P.O. Box 13398
Research Triangle Park, NC 27709

Re: NDA# 20-548
Flovent (fluticasone propionate) Inhalation Aerosol
44 mcg, 110 mcg, 220 mcg
MACMIS ID#: 6205

Dear Ms. Thompson:

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed promotional materials for Flovent (fluticasone propionate) Inhalation Aerosol 44 mcg, 110 mcg, and 220 mcg (e.g., detail aid FLO252RO 11/97) that DDMAC has determined contain claims that are false or misleading, contain unsubstantiated implied superiority claims, and lack fair balance, and therefore violate the Federal Food, Drug, and Cosmetic Act and its implementing regulations.

The detail aid contains several claims and presentations of comparative *in vivo* and *in vitro* data for various inhaled corticosteroids (ICSs):

Page One

- Headline: "High topical anti-inflammatory activity";

  Presentation of (1) comparative topical anti-inflammatory activity and
  (2) comparative corticosteroid receptor activity

  Disclaimer: "The clinical significance of the above *in vivo* and *in vitro* data has not been established."

  Intermingled/linked clinical efficacy claim: Flovent indication statement

with contraindication against acute bronchospasm

Page Two

- Headline: "Negligible (<1%) oral systemic bioavailability";
"Among inhaled corticosteroids, the majority of the inhaled dose is swallowed, while a relatively smaller proportion reaches the lungs*"

Table of comparative product percentages of swallowed portion bioavailable (% oral dose systemically bioavailable)

Flovent: (1) "Extensive first pass metabolism reduces oral systemic bioavailability to <1%"

(2) "The lowest oral bioavailability among inhaled corticosteroids"

*Footnote Qualifier: "With any inhaled corticosteroid, nearly all of the dose delivered to the lungs is bioavailable."

The overall presentation of the detail is misleading. The first page intermingles a clinical efficacy claim (Flovent indication statement with contraindication against use for acute bronchospasm) with clinical pharmacology claims in a way that suggests clinical superiority of Flovent over other ICSs based on *in vivo* and *in vitro* data, when no such clinical significance has been demonstrated.
Furthermore, even if separated from the explicit clinical efficacy claim, the comparative pharmacology presentations and claims are false or misleading. Notwithstanding the accompanying disclaimer or qualifier, these comparative pharmacology presentations imply that Flovent has superior clinical efficacy and safety to the other listed ICSs (budesonide, beclomethasone dipropionate, triamcinolone acetonide, and flunisolide) in treating asthma, based on pharmacodynamic and pharmacokinetic characteristics, rather than being demonstrated by substantial evidence (adequate and well-controlled head-to-head clinical studies). In the absence of substantial evidence, these comparative pharmacology presentations represent unsubstantiated implied clinical superiority claims.

In addition, even if presented in a noncomparative context, the implied safety claim of negligible (<1%) bioavailability lacks fair balance. According to the Pharmacokinetics:Absorption section of the Flovent approved product labeling, although the drug product's oral bioavailability is negligible (<1%), "[i]n contrast, the majority of the fluticasone propionate delivered to the lung is systemically absorbed. The systemic bioavailability of [Flovent] averaged about 30% of the dose delivered from the actuator."

DDMAC requests that the distribution and use of promotional materials containing these violative presentations cease immediately. GW's written response should be received by DDMAC no later than April 22, 1998, and should include a list of all violative materials and a description of its method of discontinuing their use.

Please direct your written 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, Maryland 20857. DDMAC reminds GW that only written communications are considered official.

In future correspondence regarding this particular matter, please refer to MACMIS ID# 6325 in addition to the NDA number.

Sincerely,

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