DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

OCT 15 1997

TRANSMITTED VIA FACSIMILE

Mr. Foma Rashovsky
Acting Director, Regulatory Affairs
Forest Laboratories, Inc.
909 Third Avenue
New York, NY 10022

RE: NDA# 18-340
Aerobid/Aerobid-M (flunisolide) Inhaler System
MACMIS ID# 4533

Dear Mr. Rashovsky:

As part of its routine monitoring activities, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed promotional materials for Aerobid/Aerobid-M (flunisolide) Inhaler System (e.g., July-August, 1997 journal ads in Chest, JAMA) and has determined that these materials are false, misleading, or otherwise lacking in fair balance and are therefore violative of the Federal Food, Drug, and Cosmetic Act and its implementing regulations. Furthermore, it appears that this particular journal ad has not been submitted as required by 21 CFR 314.8(b)(3)(i) on FDA Form-2253.

DDMAC objects to the implied safety claim in the headline/tagline "Potency that STOPS in the lungs" because it implies that this orally inhaled corticosteroid has no systemic activity or effect. However, this claim is inconsistent with the PRECAUTIONS and DOSAGE and ADMINISTRATION Sections of the approved product labeling:

> "Because of the relatively high molar dose of flunisolide per activation in this preparation, and because of the evidence suggesting higher levels of systemic absorption with flunisolide than with other comparable inhaled corticosteroids (see CLINICAL PHARMACOLOGY section), patients treated with Aerobid (flunisolide) should be observed carefully for any evidence of systemic corticosteroid effect, including suppression of bone growth in children."
>
> "The long-term and systemic effects of Aerobid in human subjects are still not fully known. In particular, the effects resulting from chronic use of Aerobid on developmental or immunologic processes in the mouth, pharynx, trachea, and lung are unknown."

> "When the drug is used chronically, at 2 mg/day, patients should be monitored periodically for effects on the hypothalamic-pituitary-adrenal (HPA) axis."

Furthermore, the safety claim headline "STRONG ON SAFETY..." is misleading because while it is supported by four bulleted claims cited to the Aerobid approved product labeling, those statements refer to nonclinical studies (i.e., clinical pharmacology model data or tests of systemic effects in human volunteers, rather than patient populations) in a way that suggests they have clinical significance when in fact no such clinical significance has been demonstrated.

Moreover, a claim included to support the efficacy "STRONG ON ASTHMA" headline is false or misleading. The bulleted claim "high topical potency for unsurpassed anti-inflammatory effect" cited to the approved product labeling (i.e., CLINICAL PHARMACOLOGY Section) suggests clinical superiority in this context, which has not been demonstrated. DDMAC is also reviewing the bulleted claim "effectively reduces and even eliminates oral steroid dependency." In a letter dated October 9, 1997, DDMAC requested the three referenced articles cited to substantiate this oral steroid-sparing claim. Upon receipt, DDMAC will review the data to establish whether this claim is adequately substantiated or violative. In subsequent correspondence under MACMIS ID# 5797, Forest will be notified of our determination on this issue.

Finally, the ad lacks fair balance by failing to present significant risk information with a prominence and readability reasonably comparable with the presentation of product benefits (i.e., above the footnote paragraph), including disclosure of side effects and contraindications.

DDMAC requests that further distribution and use of this ad and similar promotional materials cease immediately. Forest's written response should be received by DDMAC no later than October 29, 1997, and should include a list of all similarly violative materials and a description of its plan to address this issue.

Forest's response should be directed 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 Forest that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #5797 in addition to the NDA number.

Sincerely,

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