DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FEB 27 1997

TRANSMITTED VIA FACSIMILE

Ms. Kerri-Ann Arnott
Manager, Regulatory Affairs
North America
3M Pharmaceuticals
3M Center, Building 270-3A-01
St. Paul, Minnesota 55144-1000

RE: **NDA#** 20-014
Maxair Autohaler (pirbuterol acetate inhalation aerosol)
MACMIS ID# 4664

Dear Ms. Arnott:

This letter responds to a study (#013) by 3M Pharmaceuticals (3M) submitted on September 27, 1996, to the Division of Drug Marketing, Advertising, and Communications (DDMAC) in support of the following superiority claims in promotional materials for Maxair Autohaler (pirbuterol acetate inhalation aerosol) (e.g., brochure AH-2515, selectcare fact sheet AH2496).

- Headline: "50% fewer patients reported days missed from school or work"

  - "As reported in patient diaries, significantly fewer of the Maxair Autohaler patients (8%) missed days from school or work due to asthma compared with those using Maxair press and breathe inhalers (16%)" (cite 10/Study #013, Data on File)

DDMAC, in consultation with the Division of Pulmonary Drug Products (DPDP), has reviewed the promotional claims and Study #013 "The Cost-Effectiveness of 3M's Autohaler Inhalation Actuator vs a Conventional 'Press-and-Breathe' Metered Dose Inhaler (MDI)" (June 1, 1994) as substantiation for these comparative claims. We have concluded that 3M is disseminating promotional materials for Maxair Autohaler that contain statements, suggestions, or implications that are false and/or misleading in violation of the Federal Food, Drug, and Cosmetic Act and applicable regulations.

These promotional materials are violative because they make unsupported clinical superiority claims that Maxair Autohaler is more effective than Maxair "Press and Breath" Metered Dose

Inhaler (MDI) when such claims have not been demonstrated by substantial evidence (i.e., adequate and well controlled studies).

DDMAC has concluded that these claims are not substantiated by Study #013 submitted for the following reasons:

1. There was no a priori determination that the endpoints that support these claims (i.e., days missed from school or work) were the primary endpoints of the study. Because of the multiple numbers of endpoints measured in this study, and because the point estimate for the difference in days missed from school or work had a p-value of 0.032, this estimate is unlikely to be statistically significant after adjustment for multiple comparisons.

2. A baseline (pre-randomization) measurement of days missed from school or work was not made.

3. The study report does not mention the time of year (i.e., with respect to the school year) that the measurements were taken and whether this variable was controlled for in the study design.

4. Results from patients who failed treatment were not included in the analysis, and there were more treatment failures in the Autohaler group.

5. Forty patients from 2 (of the 7) investigative sites were added to the study (20 per treatment group) after an interim analysis.

For these reasons, Study #013 is not an adequate and well-controlled study to substantiate the conclusions about clinical superiority made in the above claims. Therefore, 3M should immediately cease use of any promotional materials that contain these or similar claims upon receipt of this letter. 3M should respond to this letter in writing by March 13, 1997. 3M's response should include a list of all similarly violative materials and a description of its method for discontinuing their use.

Your response and any questions should be addressed to the undersigned 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 3M that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID# 4664 in addition to the NDA number.

Sincerely,

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

File Name: maxair\daysmisd.nov

Consult:	BURKE	Date: 10/24/96, 1/6/97
Drafted:	HANKIN	Date: 1/17/97
Comment:	BURKE	Date: 2/23/97
Revised:	HANKIN	Date: 2/25/97
Concur:	ABRAMS	Date: 2/27/97

CC:
HFD-40/NDA # 20-014
HFD-40/Chron/HANKIN(2)/ABRAMS
HFD-570/NICKLAS/HONIG/JENKINS
HFD-570/NDA# 20-014

MACMIS ID# 4664

MACMIS Type Code: LETT
MACMIS Action Code: VIOL

2253 ID#: 41705 Material ID#(s): AH-2515
2253 ID#: 48535 Material ID#(s): AH2496 Selectcare fact sheet

Due Date: March 13, 1997

Close Out: N

FOI STATUS: RELEASABLE