DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FDI

Food and Drug Administration
Rockville MD 20857

MAY 7 1997

TRANSMITTED VIA FACSIMILE

Ronald J. Garutti, MD
Director, Marketed Products Support
Worldwide Regulatory Affairs
Schering Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033

Re: NDA# 20-503
Proventil-HFA (Albuterol Sulfate Inhalation Aerosol)
MACMIS # 5371

Dear Dr. Garutti:

As part of its routine monitoring activities, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed promotional materials for Proventil-HFA (Albuterol Sulfate Inhalation Aerosol) disseminated by Schering Corporation (Schering) (e.g., press release PFE0002 and brochure PF0141). DDMAC has concluded that these materials contain claims that are misleading or otherwise lack fair balance and are therefore violative of the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations.

The brochure "New Jersey State Medicaid Approved" includes the following safety claim: "In a subsequent 12-month efficacy and safety study, a statistically significant difference in the incidence of tachycardia and vomiting was not demonstrated between patients taking Proventil HFA and HFA placebo." This long-term safety claim is misleading because it minimizes the significance of the risks of tachycardia and vomiting reported for a 12-week clinical trial in the approved product labeling (for tachycardia: Proventil HFA 7%; CFC-containing propelled albuterol inhaler 2%; HFA placebo <1%); for vomiting: Proventil HFA 7%; CFC-containing propelled albuterol inhaler 2%; HFA placebo 3%). If Schering possesses long-term adverse events data it believes are adequate to supplement the 12-week clinical trial data in the approved product labeling and to provide a more complete safety profile for Proventil HFA, such data should be submitted to the Division of Pulmonary Drug Products in consideration of a labeling change.

The April 11, 1997, Schering/Key press release entitled "New Asthma Inhaler Now Available that Provides Consistent Dosing of Medication Without Releasing Ozone-Damaging CFCs" contains the following paragraph:

> "The propellant in Proventil HFA remains aerosolizable even when actuated at colder outdoor temperatures. Asthma sufferers can depend on this inhaler when they are working, vacationing or traveling. This dependability can be extremely beneficial for asthma sufferers, who may need an inhaler that is primed and ready for action when they have an asthma attack. Proventil HFA can be used as a 'rescue' medication to help asthma patients quickly -- in as little as 6 minutes -- open up constricted airway passages. Proventil HFA should be stored between 59° and 77°F."

In our launch comments, dated November 1, 1996, and December 3, 1996, DDMAC stated we would object to the chemistry claim "HFA propellant remains aerosolized (replaced by 'aerosolizable') when actuated at cold temperatures" without the addition of a reasonably prominent fair balance statement to communicate that clinical safety and effectiveness of this product stored and used at cold temperatures has not been demonstrated. The above presentation is misleading because the fair balance disclaimer has not been included. We maintain our December 3, 1996, launch comment objecting to the promotion of the "remains aerosolized when actuated at cold temperature" chemistry claim because it encourages product use under storage conditions that are inconsistent with those stated in the approved product labeling.

Furthermore, not only is such a balancing disclaimer lacking from the above presentation, but Schering has added clinical claims in association with this chemistry claim ("Asthma sufferers can depend on this inhaler when they are working, vacationing or traveling. This dependability can be extremely beneficial...."). DDMAC objected to a similar generalized clinical claim proposed on launch. Such clinical claims are misleading and lack fair balance because these claims are inconsistent with the recommended storage conditions of Proventil HFA described in the approved product labeling, and they undermine the disclaimer that clinical safety and effectiveness have not been demonstrated when the product is stored and used at cold temperatures.

DDMAC requests that the distribution and use of these materials and similar promotional materials cease immediately. Schering's written response should be received by DDMAC no later than May 21, 1997, and should include a list of all similarly violative materials and a description of its method of discontinuing their use. Schering'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 Schering that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID# 5371 addition to the NDA number.

Sincerely,

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

File Name: provthfa\2safety.nov

Drafted: HANKIN Date: 5/2/97
Concur: ABRAMS Date: 5/6/97

CC:
HFD-40/NDA# 20-503
HFD-40/Chron/Hankin(2)/Abrams
HFD-570/Johnson/Meyer
HFD-570/NDA #20-503

MACMIS ID# 5371

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MACMIS Action Code: VIOL

2253 ID#: 52032 Material ID#: PF0141 Brochure

2253 ID#: 52037 Material ID#: PFE0002 Press Release

Response Date: May 21, 1997

Close Out: N

FOI STATUS: RELEASABLE