DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

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TRANSMITTED VIA FACSIMILE

Ms. Kathryn A. Roberts
Senior Manager, Worldwide Regulatory Affairs
Rhone-Poulenc Rorer Pharmaceuticals Inc.
500 Arcola Road
P.O. Box 1200
Collegeville, PA 19426-0107

RE: **NDA# 18-117**
Azmacort (triamcinolone acetonide) Inhalation Aerosol
MACMIS ID# 6367

Dear Ms. Roberts:

This letter concerns promotional activities for Azmacort (triamcinolone acetonide) Inhalation Aerosol, including materials disseminated by Rhone-Poulenc Rorer Pharmaceuticals Inc. (RPR). The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed promotional materials (e.g., visual aid AZJ1297(6-5)A 12/97 MAZ970027), including an invitation from RPR to attendees of the upcoming American Academy of Allergy, Asthma, and Immunology (AAAAI) Annual Meeting to attend a March 12, 1998, RPR-sponsored and directed symposium entitled "Selecting an Inhaled Corticosteroid: The Role of Delivery."

According to RPR, "[a] focus of the symposium will be the use of the Positron Emission Tomography (PET) to quantify *in vivo* the deposition of an inhaled corticosteroid in the lung and provide three-dimensional deposition images...PET technology is destined to improve our understanding of drug delivery in the long-term management of asthma."

DDMAC is concerned that the March 12, 1998, symposium featuring RPR-sponsored speakers may include false and/or misleading promotional statements and implications about Azmacort similar to false and/or misleading claims and implications in the above-cited violative promotional material. DDMAC would consider such RPR-symposium statements and presentations to be in violation of the Federal Food, Drug, and Cosmetic Act (Act) and implementing regulations.

- Presentation of Nonclinical PET Imaging/Data Suggests Clinical Efficacy

The visual aid is misleading because the visual presentation of the nonclinical PET imaging data portrays deep lung drug deposition and distribution to suggest a clinical benefit when such deep lung penetration has not been correlated with clinical effect. The accompanying disclaimer "The clinical implications of these data have yet to be determined", which is not reasonably prominent and readable to the positive claims, does not remedy the overall misleading impression of clinical benefit. The clinical pharmacology PET imaging is not a validated surrogate measure of the clinical effect of orally inhaled drug products and is an inappropriate substitute for valid clinical comparisons of orally inhaled drug products. Use of such data to make implicit or explicit conclusions of clinical significance when no such clinical significance has been demonstrated is misleading.

Furthermore, written claims accompanying the PET images also misleadingly imply clinical benefit based on PET lung deposition data (e.g., on page one "New clinical evidence compares triamcinolone acetonide (TAA) deposition with and without spacer. Azmacort with the built-in spacer delivers 2 times more drug to the lungs...Proof that Azmacort--the only inhaled bronchial steroid (IBS) with a built-in spacer--delivers." Moreover, the overall presentation of these clinical pharmacology claims of *in vivo* performance of inhaled drug delivery (on pages one, four, and five) are intermingled with clinical efficacy and safety claims (on pages two and three) to further suggest that the nonclinical PET imaging data confers clinical significance in the treatment of asthma when no such significance has been demonstrated.

- Presentation of Nonclinical PET Imaging/Data Suggests Clinical Superiority

The overall presentation of the visual aid also misleadingly suggests or implies that Azmacort with a built-in spacer has superior clinical efficacy not only to Azmacort without a spacer (a product that does not exist and thus can not provide a meaningful comparator), but also to all other inhaled bronchial steroid products (which do not have built-in spacers) because of Azmacort's asserted ability to deliver twice as much medication (per puff) as an inhaled bronchial steroid without a built-in spacer. Such clinical superiority claims implying or suggesting that Azmacort is more effective than other inhaled corticosteroids administered by other types of inhaler mechanisms without a built-in spacer are false and/or misleading because they have not been demonstrated by substantial evidence (i.e., adequate and well-controlled studies).

RPR's written response should be received by March 12, 1998, and should include a list of all similarly violative materials and a description of your method for discontinuing their use. The 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 RPR that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID # 6367 in addition to the NDA number.

Sincerely,

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