DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DEC - 6 1999

TRANSMITTED VIA FACSIMILE

Dan Henry, R.Ph., Pharm.D.
Assistant Director, US Regulatory Affairs
Marketed Products
Hoechst Marion Roussel, Inc.
10236 Marion Park Drive
P.O. Box 9707
Kansas City, MO 64134-0707

RE: **NDA# 20-625**
Allegra (fexofenadine HCl) Capsules 60 mg
NDA# 20-786
Allegra-D (fexofenadine HCl 60 mg and pseuodephedrine HCl 120 mg)
Extended Release Tablets
MACMIS ID# 8268

Dear Dr. Henry:

This letter concerns a piece of homemade promotional labeling (i.e., a dear doctor letter) disseminated by a Hoechst Marion Roussel, Inc. (HMR) sales representative in August 1999 to a physician in the [ ] sales territory. This homemade promotional piece lacks fair balance and makes various express or implied unsubstantiated safety claims about Allegra (fexofenadine HCl) 60 mg Capsules and Allegra-D (fexofenadine HCl 60 mg and pseuodephedrine HCl 120 mg) Extended Release Tablets, including false or misleading claims that disparage the safety of a competitive product. The Division of Drug Marketing, Advertising, and Communications (DDMAC) has concluded that this promotional labeling violates the Federal Food, Drug, and Cosmetic Act ("Act") and its implementing regulations.

Unsubstantiated Allegra and Allegra-D Safety Superiority Claims

"...Allegra D has a delivery system that is superior to the Claritin D 12 hour. Allegra D has a wax matrix delivery of the pseudoephedrine that provides the patient with a smooth, continuous 12 hour delivery of the 120 mg. Claritin D 12 hour delivers the decongestant all at once. This "dumping" of the pseudoephedrine can exacerbate the side effects associated with pseudoephedrine."

"Finally, I believe it is important to consider the safety of Allegra, given the diversity of the patients you see. Unlike Claritin, Allegra has no dosing adjustments or special considerations in patients with hepatic impairment. Allegra works without using the P-450 system, minimizing any drug interactions. In clinical trials where Allegra was administered at 11 times the recommended dose for 28.5 days, it did not prolong the QTc interval."

Without any substantiation, these paragraphs falsely or misleadingly suggest actual or potential safety problems with the use of Claritin (loratadine) Tablets or Claritin-D 12 Hour (loratadine and pseudoephedrine sulfate) Extended Release Tablets. Similarly, these paragraphs make claims of superior product safety for Allegra or Allegra-D based on inadequate clinical evidence and/or nonclinical evidence (i.e., drug delivery system, drug metabolism as measured by pharmacokinetic parameters, including metabolism through the P-450 pathway and effect on QTc interval, or drug interactions). Such express or implied claims of superior safety for Allegra and Allegra-D have not been demonstrated by substantial evidence. Furthermore, these Allegra and Allegra-D safety superior claims lack fair balance (e.g., disclosure of adverse events) and omit material facts (i.e. a reduced dose is recommended for a starting dose in Allegra patients with decreased renal function).

On October 21, 1999, we sent HMR a written inquiry about the dissemination of this promotional material and requested a response to our questions. We also requested copies of any written or verbal communications HMR provided to its sales force that referenced any claims of actual or potential safety problems with use of Claritin or Claritin-D. On November 4 and November 11, 1999, HMR responded to DDMAC stating that the sales representative did distribute the homemade letter at issue. HMR also provided copies of corporate/training communications provided to its sales force that references Claritin or Claritin-D products.

While we acknowledge your earlier statement that the dissemination of this violative material has ceased, we remind HMR that you are responsible for assuring that your sales force's promotional activities are in compliance with the Act and its implementing regulations. DDMAC requests that HMR take the necessary steps to assure that all promotional activities by its representatives are in compliance with the Act.

Any questions or comments should be directed to the undersigned by facsimile at (301) 594-6771 or by mail at the Food and Drug Administration, Division of Drug Marketing, Advertising, and Communications, HFD-42, Rm 17-B-20, 5600 Fishers Lane, Rockville, Maryland 20857. We remind HMR that only written communications are considered official.

In future correspondence regarding this particular matter, please refer to MACMIS ID# 8268 in addition to the NDA number.

Sincerely,

/S/

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