DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

FOI

TRANSMITTED VIA FACSIMILE

Dan Henry, R.Ph., PharmD
Assistant Director, US Drug Regulatory Affairs
Marketed Products
Hoechst Marion Roussel
10236 Marion Park Drive
P.O. Box 9627
Kansas City, MO 64134-0627

FEB 23 1999

RE: **NDA 20-905**
Arava® (leflunomide) tablets
MACMIS ID # 7651

Dear Dr. Henry:

As part of its routine monitoring program, the Division of Drug Marketing, Advertising and Communications (DDMAC) has become aware of promotional materials for Arava (leflunomide) tablets disseminated by Hoechst Marion Roussel Inc.(HMR) that violate the Federal Food Drug and Cosmetic Act and its implementing regulations. Reference is made to the following promotional materials submitted under cover of form FDA 2253: Card holder (50019385/98248201/3729T8) and accompanying fact cards (50019385/98248202/3730T8, 50019385/98248203/3731T8, 50019385/98248204/3732T8, 50019385/98248205/3733T8, 50019385/98248206/3734T8, 50019385/98248207/3735T8, 50019385/98248208/3736T8, 50019385/98248209/3737T8, 50019385/98248210/3738T8). DDMAC has reviewed these materials and has determined that they promote Arava in a manner that is false or misleading because they are lacking in fair balance.

In the above referenced materials HMR presents efficacy information from U.S. clinical studies, non-U.S. clinical studies and non-U.S., non-placebo controlled clinical studies based on the ACR20 responder index. Specifically, efficacy information appears on the first three pages of the card holder and on each of the above referenced fact cards. This information appears in large point type on a blue colored background and includes several multicolored graphs and accented tables. Moreover, each one of the eight fact cards is devoted solely to the presentation of a single component of the ACR20 index. However, the only safety information presented in the piece appears on the back cover of the card holder in diminished point type on a plain white background. In addition, the information in the WARNINGS section of the approved product labeling regarding hepatotoxicity is incomplete. Guidelines for dose

adjustment or discontinuation based on severity and persistence of ALT elevations present in the WARNINGS section do not appear anywhere in the piece.

HMR should immediately cease distribution of these and other similar promotional materials for Arava that contain the same or similar claims without prominently presenting important risk information. HMR should submit a written response to DDMAC on or before March 5, 1999, describing its intent and plans to comply with the above.

HMR should direct its response to the undersigned by facsimile at (301) 827-2831, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-40; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857. DDMAC reminds HMR that only written communications are considered official.

In all future correspondence regarding this matter, please refer to MACMIS # 7651 and NDA 20-905.

Sincerely.

John C. Markow R.Ph., J.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications