DEPARTMENT OF HEALTH & HUMAN SERVICES

FOI

Food and Drug Administration
Rockville MD 20857

OCT 19 1998

TRANSMITTED VIA FACSIMILE

Thomas E. Costa
Vice President & Senior Counsel
Bristol-Myers Squibb Company
U.S. Pharmaceuticals
P.O. Box 4500
Princeton, NJ 08543-4500

Re: **NDA 19-898**
Pravachol (pravastatin sodium) Tablets
MACMIS ID # 7121

Dear Mr. Costa:

As part of its routine monitoring program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials for Pravachol (pravastatin sodium) Tablets distributed by Bristol-Myers Squibb Company (BMS) that are false or misleading in violation of the Federal Food, Drug, and Cosmetic Act and the regulations promulgated thereunder. Reference is made to two direct-to-consumer (DTC) journal advertisements submitted under cover of FDA Form 2253, one on March 11, 1998 (female swimmer) and one on September 11, 1998 (female tennis player). Upon review, DDMAC has determined that these two journal advertisements are misleading because they fail to adequately reveal facts material in light of the pictorial representations, with respect to an indicated use for Pravachol Tablets.

Pravachol is indicated for the primary prevention of coronary events. Specifically, in hypercholesterolemic patients without clinically evident coronary heart disease, Pravachol is indicated to: reduce the risk of myocardial infarction. Support for the safe and effective use of Pravachol for this indication was based on the Pravastatin Primary Prevention Study, a pivotal clinical study conducted in 6595 men, 45-64 years of age, without a previous myocardial infarction and with LDL-C levels between 156-254 mg/dL. Women were not included in this study and, in fact, the CLINICAL PHARMACOLOGY, Prevention of Coronary Heart Disease subsection of the Pravachol approved product labeling (APL) which presents a discussion of the Pravastatin Primary Prevention Study, states that, "The Pravastatin Primary Prevention Study

included only men and therefore it is not clear to what extent these data can be extrapolated to a similar population of female patients."

Each of the journal advertisements devote one full page of a two-page spread to a photograph of a woman about to participate in a strenuous sport, i.e., tennis or swimming, and each is introduced by the headline quotation, "I eat right and exercise to control my high cholesterol. Why should I worry about a first heart attack?" The facing page includes the headline, "Diet and exercise may not be enough. Pravachol reduces the risk of a first heart attack up to one-third." Implicit in these presentations is the message that women who take Pravachol will reduce their risk of a first heart attack up to one-third. However, as is specifically stated in Pravachol's product labeling, it is as yet unproved whether this particular benefit to the use of Pravachol can be duplicated in women. While BMS has included the following brief statement, buried within the running text of advertisements, that "Pravachol, in combination with diet and exercise, is proven to reduce the risk of a first heart attack, ...based on a landmark study **including over 6,500 males** with high cholesterol and no evidence of heart disease" [emphasis added], this statement alone, is not adequate to balance or qualify the misleading message presented by the full page photographs and headlines.

BMS should immediately discontinue the dissemination of these journal advertisements and any other promotional materials that contain the same or similar themes. BMS should submit a written response to DDMAC on or before November 2, 1998, confirming that BMS has discontinued the use of such material, and the date of discontinuation.

If BMS has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or in writing at DDMAC, HFD-40, Room 17B-20, 5600 Fishers Lane, Rockville MD 20857.

In all correspondence related to this matter, please refer to MACMIS ID #7121 in addition to the NDA number. DDMAC reminds BMS that only written communications are considered official.

Sincerely,

Jayne E. Peterson, R.Ph., J.D.
Regulatory Review Officer,
Division of Drug Marketing,
Advertising, and Communications