DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUL 2 1997

TRANSMITTED BY FACSIMILE

Thomas E. Costa
Vice President and Counsel
U.S. Pharmaceutical Group
Bristol-Myers Squibb Company
P.O. Box 4500
Princeton, New Jersey 08543-4500

Re: **ANDA 74-817**
Orphenadrine Citrate, Aspirin and Caffeine Tablets
(Marketed by Apothecon)
MACMIS ID #5546

Dear Mr. Costa:

This letter concerns Bristol-Myers Squibb's (BMS) promotional materials for orphenadrine, aspirin and caffeine. This product is manufactured by Invamed, Inc., and marketed by Apothecon (a Bristol-Myers Squibb Company). In our telephone conversation on July 2, 1997, you stated that BMS was responsible for the promotional materials for this product and that you should be the contact person for this issue.

The Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed, as part of its monitoring program, promotional labeling materials disseminated by BMS by mail. These materials stated that orphenadrine citrate, aspirin and caffeine tablets manufactured by Invamed and distributed by Apothecon are "AB Rated, Therefore Bioequivalent to Norflex." This statement is false and raises serious concerns about potentially dangerous use of this product. Thus, BMS is in violation of the Federal Food, Drug, and Cosmetic Act (Act) and regulations promulgated thereunder.

The products marketed by Apothecon comprise combinations of orphenadrine citrate, aspirin and caffeine. However, Norflex contains only a single active agent, namely, orphenadrine citrate. Thus, these products are not AB rated and are not bioequivalent. There is significant risk and potential danger to consumers if Apothecon's product were used inadvertently in place of Norflex by a consumer who is allergic to aspirin or who has peptic ulcers or coagulation abnormalities.

BMS should provide a written response to DDMAC by July 3, 1997, indicating that the dissemination of these materials and all other materials containing such representations has been discontinued.

In addition, BMS should immediately, clearly, and prominently alert health care professionals of this serious error, that its orphenadrine citrate, aspirin and caffeine tablets are not bioequivalent to Norflex, and the potential risks of using this product by aspirin sensitive individuals. BMS should present a proposal for how it proposes to disseminate this message.

Finally, in reviewing our files, DDMAC was unable to locate copies of these promotional materials. BMS should submit copies of all promotional materials disseminated in regard to the Apothecon products discussed in this letter and should inform DDMAC of the date that these promotional materials were submitted under Form 2253. Section 314.81(b)(3) requires that the applicant submit two copies of labeling or advertising devised for promotion of the drug product at the time of initial dissemination or publication.

BMS should direct its response to the undersigned at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm 17B-20, 5600 Fishers Lane, Rockville, MD, 20857. DDMAC reminds BMS that only written communications are considered official.

In all future correspondence regarding this matter, please refer to MACMIS ID #5546, in addition to the NDA number.

Sincerely,

Stephen W. Sherman

Stephen W. Sherman, MBA
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications