DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 19-898/S-031

JUN - 9 2000

Bristol-Myers Squibb Pharmaceutical Research Institute
Attention: Fred Henry
Director, Global Regulatory Strategy
P.O. Box 4000
Princeton, NJ 08543

Dear Mr. Henry:

Please refer to your supplemental new drug application dated March 18, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Pravachol (pravastatin sodium) Tablets.

We acknowledge receipt of your submissions dated April 3, 2000, received April 4, 2000, which constituted a complete response to our January 18, 2000, action letter. We also acknowledge receipt of your May 11 (fax), 2000, submission.

This supplemental new drug application provides for the additional indication of increasing HDL-C in patients with primary hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (Frederickson Types IIa and IIb). The INDICATIONS AND USAGE, "Hyperlipidemia" section of the package insert for Pravachol will state "Pravachol is indicated as an adjunct to diet to reduce elevated total-C, LDL-C, apo B, and TG levels ***and to increase HDL-C*** in patients with primary hypercholesterolemia (heterozygous familial and nonfamilial) and mixed dyslipidemia (Frederickson Types IIa and IIb)." *(Italics indicate the change.)* In addition, this change is reflected in the CLINICAL PHARMACOLOGY section of the package insert by deletion of the word "variable" in the description of the HDL-raising effect of pravastatin and by inclusion of summary data on the HDL-C changes observed in the WOS and CARE trials.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted May 11, 2000.)

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 19-898/S-031." Approval of this submission by FDA is not required before the labeling is used.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that a Written Request (WR) for pediatric studies in patients with heterogygous familial hypercholesterolemia (heFH) was sent to you on August 4, 1999. No specific studies in Frederickson Type IIa and IIb are required. We hereby waive the requirement for pediatric studies in these groups, and we defer submission of the pediatric studies in heFH until March 31, 2002.

Submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Margaret Simoneau, R.Ph., Regulatory Management Officer, at (301) 827-6418.

Sincerely,

/S/

John K. Jenkins, M.D.
Acting Director
Division of Metabolic and Endocrine
Drug Products, HFD-510
Office of Drug Evaluation II
Center for Drug Evaluation and Research