DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-898/S-046

Bristol-Myers Squibb
Attention: Porter P. Layne, Ph.D.
Group Director, Metabolic/Endocrine Products
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Dr. Layne:

Please refer to your supplemental new drug application dated March 1, 2001, received March 1, 2001, 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 4, 11, 16, and 20, June 7, August 9 and 17, September 18, 20, and 27, October 2, 25 (2), and 30, November 6, and December 5 (2), 10, 11, and 13, and 17, 2001.

This supplemental new drug application provides for the use of a new dosage strength (80 mg) and dosing regimen (80 mg once per day) of Pravachol (pravastatin sodium) tablets.

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 enclosed 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 enclosed labeling (text for the package insert submitted on December 17, 2001) and submitted draft labeling (immediate container and carton labels submitted March 1, 2001).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no 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-046." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitment in your submission dated December 10, 2001 and amended December 13, 2001. This commitment is listed below.

> Submission by April 30, 2002, of the final study report for Period C (long-term extension) of study CV123-231, which will provide additional safety information on daily administration of 80 mg and 160 mg of Pravachol. Revisions to the Pravachol label may be needed after review of these data.

Submit clinical protocols to your IND for this product. Submit all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

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 (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55. We are waiving this requirement for patients from 0 to 7 years of age and are deferring submission of your pediatric studies, with doses from 10 mg to 40 mg/day for patients aged 8 through 17 years, until March 31, 2002. We are deferring studies of 80 mg pravastatin/day for pediatric patients aged 8 through 17 years until November 30, 2006.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. We note that we have issued a Written Request dated August 4, 1999, amended May 29, 2001, and your studies must be submitted by March 31, 2002.

In addition, please 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-42
> 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 Professional" 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 Project Manager, at (301) 827-6411.

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure