DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 9-218/S-101

Bristol-Myers Squibb Company
Attention: David L. Silberstein
Associate Director
New Opportunities and Product Development
Global Regulatory Strategy
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Mr. Silberstein:

Please refer to your supplemental new drug application dated April 6, 2005, received April 7, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for COUMADIN® Tablets (Warfarin Sodium Tablets, USP) Crystalline and COUMADIN® for Injection (Warfarin Sodium for Injection, USP).

This "Changes Being Effected" supplemental new drug application provides for revisions to the Coumadin package insert to include information relating to drug interactions with Proton Pump Inhibitors (PPIs) and language cautioning against the ingestion of cranberry products, which have been reported to affect the response of patients to Coumadin.

We completed our review of this application. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text with the correction listed below.

> In the seventh paragraph, first sentence of the **DOSAGE AND ADMINISTRATION s**ection that reads "An INR of greater than 4.0 appears to provide no additional therapeutic benefit in most patients and is associated with a higher risk of bleeding." in the final printed labeling (FPL) to this supplement, retain the bolding, as in the currently approved labeling.

The FPL must be identical, and include the revision indicated, to the enclosed labeling (text for the package insert) and/or submitted labeling (package insert submitted April 6, 2005). This revision is a term of the approval of this application.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. 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. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplement NDA 9-218/S-101**." Approval of this submission by FDA is not required before the labeling is used.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Diane Moore, Regulatory Project Manager, at (301) 827-7476.

Sincerely,

{See appended electronic signature page}

Joyce Korvick, M.D., M.P.H.
Deputy Division Director
Division of Gastrointestinal and Coagulation Drug Products (HFD-180)
Office of Drug Evaluation III
Center for Drug Evaluation and Research

enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Kathy Robie-Suh
9/2/2005 02:46:13 PM
signing for Dr. Joyce Korvick