DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-986

Bristol-Myers Squibb Company
Attention: Marie-Laure Papi, Pharm.D.
Associate Director, Regulatory Science
5 Research Parkway
P.O. Box 5100, Mailstop 3SIG-5014
Wallingford, CT 06492

Dear Dr. Papi:

Please refer to your new drug application (NDA) dated December 28, 2005, received December 28, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for SPRYCEL™ (dasatinib) Tablets.

We acknowledge receipt of your submissions dated February 15 and 23 (2); March 7, 21, 22 and 30; April 5, 6, 7, 13, 17, 18, 25, 26 and 27 (2); May 2 (2) and June 16, 2006.

This new drug application provides for the use of SPRYCEL™ (dasatinib) Tablets for the treatment of adults with chronic myeloid leukemia with resistance or intolerance to prior therapy including imatinib.

We completed our review of this application, as amended. It is approved under the provisions of accelerated approval regulations (21 CFR 314.510), effective on the date of this letter, for use as recommended in the enclosed labeling text and patient labeling. Marketing of this drug product and related activities must adhere to the substance and procedures of the referenced accelerated approval regulations.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, text for the patient package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 NDA 21-986**." Approval of this submission by FDA is not required before the labeling is used.

Submit content of labeling [21 CFR 601.14(b)] in structured product labeling (SPL) format, as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed

labeling text. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

Products approved under the accelerated approval regulations, 21 CFR 314.510, require further adequate and well-controlled studies to verify and describe clinical benefit. We remind you of your post marketing study commitments specified in your submission dated June 27, 2006. These commitments, along with any completion dates agreed upon, are listed below.

1. You have agreed to submit the complete study report and data from the study, CA-180-002, a bicenter, dose escalation study to determine the safety, pharmacokinetics, and pharmacodynamics of BMS-354825 in the treatment of patients with Chronic, Accelerated, or Blast Phase Chronic Myelogenous Leukemia, or Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia who have hematologic resistance to Imatinib Mesylate.

   Protocol Submission: 03/2003
   Study Start: 11/2003
   Final Report Submission: 06/2007

2. You have agreed to submit the complete study report (24 months follow-up) and data from the study, CA-180-005, a phase 2 multicenter study of dasatinib (BMS-354825) in subjects with Accelerated Phase Chronic Myeloid Leukemia resistant to or intolerant of Imatinib Mesylate.

   Protocol Submission: 11/2004
   Study Start: 12/2004
   Final Report Submission: 06/2008

3. You have agreed to submit the complete study report (24 months follow-up) and data from the study, CA-180-006, a phase 2 multicenter study of dasatinib (BMS-354825) in subjects with Myeloid Blast Phase Chronic Myeloid Leukemia resistant to or intolerant of Imatinib Mesylate.

   Protocol Submission: 11/2004
   Study Start: 12/2004
   Final Report Submission: 06/2008

4. You have agreed to submit the complete study report (24 month follow-up) and data from the study, CA-180-013, a phase 2 multicenter study of dasatinib (BMS-354825) in subjects with Chronic Phase Philadelphia Chromosome Positive Chronic Myeloid Leukemia who have disease that is resistant to high dose Imatinib Mesylate or who are intolerant of Imatinib Mesylate.

   Protocol Submission: 11/2004
   Study Start: 02/2005
   Final Report Submission: 06/2008

5. You have agreed to submit the complete study report (24 month follow-up) and data from the study, CA-180-017, a randomized, open-label multicenter study of dasatinib (BMS-354825) versus Imatinib Mesylate (Gleevec, Glivec) 800 mg/d in subjects with Chronic Phase Philadelphia Chromosome Positive Chronic Myeloid Leukemia who have disease that is resistant to Imatinib Mesylate at a Dose of 400 - 600 mg/d.

   Protocol Submission: 11/2004
   Study Start: 02/2005
   Final Report Submission: 12/2008

6. You have agreed to submit the complete study report (24 month follow-up) and data from the study, CA-180-015, a phase 2 multicenter study of dasatinib (BMS-354825) in subjects with Lymphoid Blast Phase Chronic Myeloid Leukemia or Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia resistant to high dose Imatinib Mesylate (Gleevec) or who are intolerant of Imatinib Mesylate.

   Protocol Submission: 11/2004
   Study Start: 01/2005
   Final Report Submission: 06/2008

Submit final study reports to this NDA as a supplemental application. For administrative purposes, all submissions relating to these postmarketing study commitments must be clearly designated "**Subpart H Postmarketing Study Commitments**."

In addition, we note your following postmarketing study commitments, specified in your submission dated June 27, 2006, that are not a condition of the accelerated approval. These commitments are listed below:

7. You have agreed to submit the completed study report (24 month follow-up) and data from the study, CA-180-034, a randomized, two-by-two, open-label study of dasatinib (BMS-354825) in subjects with Chronic Phase Philadelphia Chromosome Positive Chronic Myeloid Leukemia resistant to or intolerant of Imatinib Mesylate.

   Protocol Submission: 04/2005
   Study Start: 07/2005
   Final Report Submission: 06/2009

8. You have agreed to submit the complete study report and data from the study, CA-180-051, a single-dose, pharmacokinetic study of BMS-354825 in subjects with hepatic impairment compared to healthy adult subjects.

   Protocol Submission: 05/2006
   Study Start: 10/2006
   Final Report Submission: 01/2009

9. You have agreed to submit the complete study report and data from the study, CA-180-021, an open-label, single-sequence study to evaluate the effect of ketoconazole on the pharmacokinetics of BMS-354825 in patients with advanced solid tumors.

   Protocol Submission: 03/2005
   Study Start: 07/2005
   Final Report Submission: 12/2006

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and 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 Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

As required by 21 CFR 314.550, submit all promotional materials at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement. Send two copies of all promotional materials directly to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

In addition, as required by 21 CFR 314.550, submit all subsequent promotional materials at least 30 days before the intended time of initial distribution of labeling or initial publication of the advertisement. Send two copies of the promotional materials and the package insert to the address above.

Please submit one market package of the drug product when it is available.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

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

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Amy Baird, Consumer Safety Officer, at (301) 796-1325.

Sincerely,

{See appended electronic signature page}

Richard Pazdur, M.D.
Director
Office of Oncology Drug Products
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/

Karen Weiss
6/28/2006 03:59:16 PM
for Dr. Richard Pazdur