DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-588/S011, S012, S013, S014, S017

Novartis Pharmaceuticals Corporation
Drug Regulatory Affairs
One Health Plaza, Bldg. 105/Rm. 2W200
East Hanover, NJ 07936-1080

Attention: Joseph Quintavalla
Senior Regulatory Manager Drug Regulatory Affairs

Dear Mr. Quintavalla:

Please refer to your supplemental new drug applications identified below, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Gleevec (imatinib mesylate) Tablets.

SUPP #	LETTER DATE	RECEIPT DATE	PROVIDES FOR THE TREATMENT OF
S011	December 16, 2005	December 19, 2005	adult dermafibrosarcoma protuberans (DFSP)
S012	December 16, 2005	December 19, 2005	adult myelodysplastic syndrome/myeloproliferative diseases (MDS/MPD)
S013	December 20, 2005	December 21, 2005	adult Ph+ acute lymphoblastic leukemia (ALL) monotherapy
S014	February 28, 2006	March 1, 2006	adult aggressive systemic mastocytosis (ASM)
S017	March 28, 2006	March 29, 2006	adult hypereosinophilic syndrome/chronic eosinophilic leukemia (HES/CEL)

We acknowledge receipt of your submissions dated January 24, 2006; February 6, 2006; April 7, 10, 2006; May 15, 18, and 24, 2006; and September 25, 2006.

We have completed our review of these supplemental applications, as amended. These supplemental applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and/or submitted labeling.

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 supplements NDA 21-588/S011, S012, S013, S014, S017**." 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.

We remind you of your postmarketing study commitments in your submission dated September 25, 2006 and amended in your e-mail communication of October 13, 2006. These commitments are listed below.

1. (for S012) To meet with the Division and the FDA Center for Devices and Radiological Health (CDRH) Office of In Vitro Diagnostics within 3 months to discuss the feasibility of a validated test kit for PDGFR gene rearrangements for patients with MDS/MPD.

2. (for S014) To meet with the Division and the FDA CDRH Office of In Vitro Diagnostics within 3 months and propose a plan with timelines thereafter for the development of a validated test kit for the detection of the D816V c-kit mutation in aggressive systemic mastocytosis.

3. (for S017) To meet with the Division and FDA CDRH Office of In Vitro Diagnostics within 3 months and propose a plan with timelines thereafter for the development of a validated test kit for the detection of the FIP 1L1-PDGFR-alpha fusion protein in HES/CEL.

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**."

Open commitments under NDA 21-588:

Prior commitment required for accelerated approval of Gleevec for newly diagnosed pediatric CML patients (NDA 21- 588/016 submitted March 27, 2006 and approved September 27, 2006):

1. To [provide] follow up safety and efficacy information for Study 2108. Updated status reports to be submitted in March 2007 and March 2008. Provision of further long term data will be re-assessed following the submission of the March 2008 study status report and will depend on the number of patients still on study at that time.

Prior commitment required for accelerated approval of Gleevec for GIST patients (NDA 21-335/001 submitted October 15, 2001 and approved February 1, 2002):

4. Submit data from the two ongoing multicenter trials of imatinib that are testing 400 mg/day versus 800 mg/day in patients with GIST (EORTC and NCI sponsored trials). Response rate, duration of response, safety and survival data should be submitted. The data should be submitted in a timeline consistent with the statistical analysis plan of each respective protocol.

Prior commitment required for accelerated approval of Gleevec for newly diagnosed CML patients (NDA 21-335/004 submitted June 28, 2002 and approved December 20, 2002):

7. To provide interval follow-up safety and efficacy information on study 106 annually, for three additional years, and survival data and serious adverse event data thereafter for another three years. Timeline: First interval report submitted on December 22, 2003 and to be submitted annually thereafter until January 2009.

We also remind you of your postmarketing commitments which are not a condition of accelerated approval.

Prior commitments which are not a condition of accelerated approval of Gleevec for CML patients (NDA 21-335/000 submitted February 1, 2001 and approved May 10, 2001):

11. To conduct the appropriate study to assess the potential drug interaction between Gleevec and a substrate of CYP2D6 and to submit the final study report.

14. To evaluate the etiology and treatment of the fluid retention syndrome associated with imatinib treatment.

    We refer to your submission of September 5, 2006 regarding this commitment. This submission is under review by FDA.

Prior commitment which is not a condition of accelerated approval of Gleevec for GIST patients (NDA 21-335/001 submitted October 15, 2001 and approved February 1, 2002):

15. Submit the PK/PD data from the comparison of 400 mg/day versus 800 mg/day in GIST patients in the two ongoing multicenter trials of imatinib (EORTC and NCI sponsored trials).

Prior commitment which is not a condition of accelerated approval of Gleevec for newly diagnosed CML patients (NDA 21-335/004 submitted June 28, 2002 and approved December 20, 2002):

18. To conduct a prospective study performed in patients receiving both Gleevec and a potent CYP3A4 inducer such as phenytoin, phenobarbital, or carbamazepine and submit a final study report. The purpose of this study is to determine the dose of Gleevec that is necessary to produce similar AUCs in these patients on enzyme inducers to those achieved in adult patients receiving the usual recommended dose (400 mg/day). Timeline: Protocol submission June 2003; study start date December 2003; and final report December 2004.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send two copies of both the promotional materials and the package insert 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

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
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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 Dotti Pease, Regulatory Project Manager, at (301) 796-1434.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D.
Director
Division of Drug Oncology Products
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/

Robert Justice

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