**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-938/S-002/S-003/S-004/S-005
NDA 21-968/S-002/S-003/S-004/S-005/S-006

C.P. Pharmaceuticals International C.V.
c/o Pfizer, Inc.
10646 Science Center Drive
San Diego, CA 92121

Attention: Laurie M. Strawn, Ph.D.
Director, Worldwide Regulatory Strategy

Dear Dr. Strawn:

Please refer to your supplemental new drug applications dated March 30, March 31, August 1, and August 9, 2006, received March 31, April 3, August 2, and August 11, 2006, respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for SUTENT® (sunitinib malate) Capsules, 12.5 mg, 25 mg, and 50 mg sunitinib equivalent.

We acknowledge receipt of your submissions dated May 23, August 1 and 16 (2), September 26 and 29 (2), October 2 (5), 10, and 13, November 17 (2), 21, and 28, December 5 and 12, 2006, and February 1, 2007.

NDA 21-938/S-002 and NDA 21-968/S-002 were submitted in response to postmarketing commitment #7 from the January 26, 2006, approval letter, and provide for revisions to the labeling based on data from the study titled, *"A Phase 1 Study to Evaluate the Effect of SU011248 on QTc Interval in Subjects with Advanced Solid Tumors"*.

NDA 21-938/S-003 and NDA 21-968/S-003 and S-004 were submitted in response to postmarketing commitments #1 and #3 from the January 26, 2006, approval letter and provide for revisions to the labeling based on data from the first interim efficacy and safety analysis for the study titled, *"A Phase 3, Randomized Study of SU011248 versus Interferon-α as First-Line Systemic Therapy for Patients with Metastatic Renal Cell Carcinoma"*. The supplements also provide the datasets containing the core imaging facility assessments used to derive the updated response rate for the study titled, *"A Pivotal Study of SU011248 in the Treatment of Patients with Cytokine-Refractory Metastatic Renal Cell Carcinoma"*.

NDA 21-938/S-004 and NDA 21-968/S-005 were submitted in response to postmarketing commitments #2 and #4 from the January 26, 2006, approval letter and provide for revisions to the labeling based on data from the final study report for the study titled, *"A Phase 3, Randomized Study of SU011248 versus Interferon-α as First-Line Systemic Therapy for Patients with Metastatic Renal Cell Carcinoma"*. The supplements also provide follow-up left ventricular ejection fraction (LVEF) data for selected patients on the study titled, *"A Pivotal Study of SU011248 in the Treatment of Patients with Cytokine-Refractory Metastatic Renal Cell Carcinoma"*.

NDA 21-938/S-005 and NDA 21-968/S-006 were submitted in response to postmarketing commitment #8 from the January 26, 2006, approval letter and provide for revisions to the labeling based on data from the final study report for the study titled, *"A Phase I Study to Evaluate the Pharmacokinetics of SU011248 in Subjects with Impaired Hepatic Function"*.

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

Within 21 days of the date of this letter, submit content of labeling [21 CFR 314.50(l)] 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. Upon receipt and verification, we will transmit that version to the National Library of Medicine for public dissemination.

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

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 these submissions "**FPL for approved supplements NDA 21-938/S-002/S-003/S-004/S-005 and NDA 21-968/S-002/S-003/S-004/S-005/S-006**." Approval of these submissions by FDA is not required before the labeling is used.

We approved NDA 21-968 under the regulations at 21 CFR 314 Subpart H for accelerated approval of new drugs for serious or life-threatening illnesses. Approval of NDA 21-968/S-005 fulfills the following commitments made under 21 CFR 314.510.

1. Provide the response rate and duration of response data from the first interim efficacy analysis of study titled "A Phase 3, Randomized Study of SU011248 versus Interferon-α as First-Line Systemic Therapy for Patients with Metastatic Renal Cell Carcinoma". Also, submit the comparative safety data that are available at the time of data cutoff for the interim analysis. This will include an interim study report as well as raw and derived datasets.

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   | Protocol Submission: | submitted 06/2004 |
   | Study Start: | 08/2004 |
   | Final Report Submission: | by 03/2006 |

2. Submit efficacy data obtained at the final analysis, including progression-free survival, overall survival, response rate and duration of response; as well as updated safety data for study titled "A Phase 3, Randomized Study of SU011248 versus Interferon-α as First-Line Systemic Therapy for Patients with Metastatic Renal Cell Carcinoma". This submission will include the final study report as well as raw and derived data sets.

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   | Protocol Submission: | submitted 06/2004 |
   | Study Start: | 08/2004 |
   | Final Report Submission: | by 07/2006 |

3. Submit raw and derived datasets containing the core imaging facility assessments used to derive the updated response rate and median duration of response on study titled "A Pivotal Study of SU011248 in the Treatment of Patients with Cytokine-Refractory Metastatic Renal Cell Carcinoma".

   Protocol Submission: submitted 11/2003
   Study Start: 02/2004
   Final Report Submission: by 03/2006

4. Submit follow-up left ventricular ejection fraction (LVEF) data for patients 16, 46, and 81 on the study titled "A Pivotal Study of SU011248 in the Treatment of Patients with Cytokine-Refractory Metastatic Renal Cell Carcinoma". Case narratives should be submitted and should include additional cardiac evaluations that were performed and treatments that were administered for congestive heart failure. Additionally, submit LVEF data and clinical narratives for any patient who, after the data cutoff for the initial NDA submission, had a documented LVEF of ≤ 40% and/or signs and symptoms of cardiac failure.

   Protocol Submission: submitted 11/2003
   Study Start: 02/2004
   Final Report Submission: by 05/2006

In addition, we have concluded that the following postmarketing commitments from the January 26, 2006, approval letter have also been fulfilled:

7. Submit the completed report and datasets for study titled "A Phase 1 Study to Evaluate the Effect of SU011248 on QTc Interval in Subjects with Advanced Solid Tumors".

   Protocol Submission: submitted 07/2004
   Study Start: 08/2004
   Final Report Submission: by 03/2006

8. Submit the completed report and datasets for study titled "A Phase 1 Study to Evaluate the Pharmacokinetics of SU011248 in Subjects with Impaired Hepatic Function".

   Protocol Submission: submitted 08/2005
   Study Start: 09/2005
   Final Report Submission: by 05/2006

Finally, we have reviewed your submission dated September 26, 2006, and conclude that the following commitment from the January 26, 2006, approval letter was fulfilled.

6. Provide an analysis of the relationship between exposure and efficacy outcomes from the study titled "A Phase 3, Randomized Study of SU011248 versus Interferon-α as First-Line Systemic Therapy for Patients with Metastatic Renal Cell Carcinoma".

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   | Protocol Submission: | submitted 06/2004 |
   | Study Start: | 08/2004 |
   | Final Report Submission: | by 07/2006 |

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 are waiving the pediatric study requirement for this application.

We remind you of your postmarketing study commitment in your electronic mail submission dated February 1, 2007, listed below.

1. Provide the complete study report and datasets with the final definitive statistical analysis of overall survival and duration of response for the study titled, "A Phase 3, Randomized Study of SU011248 versus Interferon-alpha as First-Line Systemic Therapy for Patients with Metastatic Renal Cell Carcinoma".

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   | Protocol Submission: | submitted 6/2004 |
   | Study Start: | 8/2004 |
   | Final Report Submission: | 2/2009 |

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to NDA 21-938. 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 NDA 21-938. 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**."

We also remind you of your outstanding postmarketing study commitments from the January 26, 2006, approval letter. These commitments are listed below. Note that postmarketing study commitment #5 is no longer considered required under the regulations at 21 CFR 314 Subpart H.

5. Submit comparative LVEF and cardiac safety data for patients enrolled on the adjuvant renal cell carcinoma trial, E2805 titled "A Randomized, Double-Blind Phase III Trial of Adjuvant Sunitinib versus Sorafenib versus Placebo in Patients with Resected Renal Cell Carcinoma". The protocol will be revised to include a plan acceptable to the FDA for ejection fraction monitoring at baseline and follow-up.

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| Initial Protocol Submission: | submitted 11/2005 |
| Revised Protocol Submission: | by 05/2006 |
| Study Start: | by 03/2006 |
| Final Report Submission: | by 06/2011 |

9. Submit completed final study report for study titled "A Phase III, Randomized, Double-Blind, Placebo-Controlled Study of SU011248 in the Treatment of Patients with Imatinib Mesylate (Gleevec®, Glivec®)-Resistant or Intolerant Malignant Gastrointestinal Stromal Tumor".

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| Protocol Submission: | submitted 11/2003 |
| Study Start: | 12/2003 |
| Final Report Submission: | by 12/2006* |

* Note that this postmarketing study commitment is considered 'delayed' according to 21 CFR 314.81(b)(2)(vii)(8). However, we acknowledge your current projected completion date of 12/2007 for this commitment.

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 NDA 21-938 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 Christy Cottrell, Consumer Safety Officer, at (301) 796-1347.

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

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

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/s/
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Robert Justice
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