DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021938/S-013/S-017/S-018

SUPPLEMENT APPROVAL
RELEASE REMS REQUIREMENT

C.P. Pharmaceuticals International C.V.
c/o Pfizer, Inc.
235 East 42nd Street
New York, NY 10017

Attention: Ann Carey
Senior Director, Worldwide Regulatory Strategy

Dear Ms. Carey:

Please refer to your Supplemental New Drug Applications (sNDA) dated July 28 (S-017), December 3 (S-013) and December 8, 2010 (S-018), received July 28, December 3, and December 8, 2010, respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Sutent® (sunitinib malate) Capsules.

We acknowledge receipt of your amendments dated December 20, 2010, January 26, February 11, April 25, and May 17, 2011. The December 3, 2010, submission (S-013) constituted a complete response to our May 28, 2010, action letter.

"Prior Approval" supplemental new drug application S-013 provides for a new indication for the treatment of progressive, well-differentiated pancreatic neuroendocrine tumors in patients with unresectable, locally advanced, or metastatic disease.

"Prior Approval" supplemental new drug application S-017 provides for updates to the Warnings and Precautions, Use in Specific Populations, Clinical Pharmacology, and Nonclinical Toxicology sections of the package insert as requested by the FDA in a supplement request letter dated May 28, 2010. Specifically, the proposed revisions incorporate findings from the rat pre- and post-natal development study, rasH2 transgenic mouse carcinogenicity studies and a Phase 1 renal impairment study.

"Prior Approval" supplemental new drug application S-018 provides for updates to the Warnings and Precautions and Adverse Reactions sections of the package insert as well as the Medication Guide to incorporate text regarding wound healing and arterial thromboembolic events.

We also acknowledge receipt of your amendment dated April 25, 2011, which proposed to eliminate the requirement for the approved risk evaluation and mitigation strategy (REMS) and contained your assessment of the Sutent® REMS.

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

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

The REMS for Sutent® (sunitinib malate) Capsules was originally approved on July 1, 2010. The REMS consists of a Medication Guide and a timetable for submission of assessments of the REMS.

You propose that FDA no longer require a REMS for Sutent® (sunitinib malate) Capsules.

We have determined that maintaining the Medication Guide as part of the approved labeling is adequate to address the serious and significant public health concern and meets the standard in 21 CFR 208.1. Therefore, it is no longer necessary to include the Medication Guide as an element of the approved REMS to ensure that the benefits of Sutent® (sunitinib malate) outweigh its risks, and we agree that a REMS for Sutent® (sunitinib malate) Capsules is no longer required.

We remind you that the Medication Guide will continue to be part of the approved labeling in accordance with 21 CFR 208.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert and Medication Guide), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable. Pancreatic neuroendocrine tumors are extremely rare in the pediatric population making it prohibitive to effectively conduct a clinical trial in the pediatric population.

POSTMARKETING REQUIREMENTS UNDER 505(o) for S-013

Section 505(o)(3) of the FDCA authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute.

Since Sutent® (sunitinib malate) Capsules were approved on January 26, 2006, we have become aware of a clinical trial in which information on overall survival has not been reported. A decrease in overall survival of patients treated with Sutent® (sunitinib malate) Capsules would change the safety profile of this drug for this indication. We consider this information to be "new safety information" as defined in section 505-1(b)(3) of the FDCA.

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess the signal of a serious risk of a decrease in overall survival of patients treated with Sutent® (sunitinib malate) Capsules.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA will not be sufficient to assess this serious risk.

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess the signal of a serious risk of a decrease in overall survival of patients treated with Sutent® (sunitinib malate) Capsules.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following:

1765-1: Submit the results of the 5-year follow-up analysis of overall survival data from the randomized clinical trial of sunitinib 37.5 mg vs. placebo in pancreatic neuroendocrine tumors (Study A6181111).

The timetable you submitted on April 26, 2011, states that you will conduct this trial according to the following schedule:

Trial Completion:	May 2014
Final Report Submission:	December 2014

Submit all updates and final reports to this NDA. Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission, as appropriate: **"Required Postmarketing Final Report Under 505(o)", "Required Postmarketing Correspondence Under 505(o)"**.

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trials required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B for S-013

We remind you of your postmarketing commitments for S-013:

1765-2: Conduct a clinical trial of patients with progressive, locally advanced or metastatic, treatment-naive or previously treated pancreatic neuroendocrine tumors (pNET) to verify and describe the efficacy and safety of sunitinib.

The timetable you submitted on April 26, 2011, states that you will conduct this trial according to the following schedule:

Final Protocol Submission:	July 2011
Trial Completion:	June 2016
Final Report Submission:	December 2016

Submit clinical protocols to your IND 062382 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 studies/clinical trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) 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

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

REPORTING REQUIREMENTS

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, Regulatory Project Manager, at (301) 796-4256.

Sincerely,

{See appended electronic signature page}

Robert L. Justice, M.D., M.S.
Director
Division of Drug Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

ROBERT L JUSTICE
05/20/2011