DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Our STN: BL 125147/26

JUN 23 2008

Amgen, Incorporated
Attention: Randy Fenrick, Ph.D., M.B.A.
Senior Manager, Global Regulatory Affairs and Safety
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

Dear Dr. Fenrick:

Your request to supplement your biologics license application for Panitumumab (Vectibix) to include a summary of the trial design and results of the 20040249 (PACCE) study in the Clinical Studies section of the package insert has been approved.

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

Accelerated Approval (Subpart E)

Vectibix was approved under the surrogate endpoint provisions of the accelerated approval regulations, 21 CFR 601.40-46 (Subpart E). Products approved under these provisions of Subpart E require further adequate and well-controlled trials to verify and describe clinical benefit. We remind you of your postmarketing requirement specified in your submission dated September 22, 2006 and as stated in our approval letter dated September 27, 2006. This requirement is listed below.

1. "To submit a final study report for study 20050181, entitled, "A Randomized, Multicenter Phase 3 Study to Compare the Efficacy of Panitumumab in Combination with Chemotherapy to the Efficacy of Chemotherapy Alone in Patients with Previously Treated Metastatic Colorectal Cancer," which is intended to verify the clinical benefit of Panitumumab through demonstration of an effect on overall survival (OS). This protocol was accepted for Special Protocol Assessment on May 3, 2006. Patient accrual began on June 30, 2006 and will be completed by September 30, 2009. The final study report will be submitted by March 30, 2010."

Submit the final report to this BLA as a supplemental application. For administrative purposes, all submissions relating to this postmarketing requirement must be clearly designated "**Subpart E Postmarketing Requirements.**"

POSTMARKETING REQUIREMENTS UNDER 505(o)

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Act of 2007 (FDAAA) amends the Federal Food, Drug, and Cosmetic Act (FDCA) to authorize 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 (section 505(o)(3)(A), 21 U.S.C. 355(o)(3)(A)). This provision took effect on March 25, 2008.

Since Vectibix was approved on September 27, 2006, for the treatment of EGFR-expressing metastatic colorectal carcinoma with disease progression on or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens, we have become aware of higher morbidity, shorter survival, and shorter progression-free survival in patients treated with Vectibix in combination with Avastin and chemotherapy. This information was not available when Vectibix was granted marketing authorization for the treatment of EGR-expressing metastatic colorectal carcinoma with disease progression. Therefore, we consider this information to be "new safety information" as defined in FDAAA.

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 a signal of a serious risk, that is, decreased survival with the concomitant use of panitumumab (Vectibix) and chemotherapy.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA has not yet been established and is not sufficient to assess this signal of a serious risk.

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to assess this signal of a serious risk.

Therefore, based on appropriate scientific data, FDA has determined that you are required, pursuant to section 505(o)(3) of the FDCA, to conduct the following clinical trial:

2. To complete and provide a final Clinical Trial Report for Study 20050203: First-line Treatment entitled, "A Randomized, Multicenter, Phase 3 Study to Compare the Efficacy of Panitumumab in Combination with Oxaliplatin/ 5-fluorouracil/leucovorin to the Efficacy of Oxaliplatin/5-fluorouracil/leucovorin Alone in Patients with Previously Untreated Metastatic Colorectal Cancer," including a final analysis of any significant toxicities that have occurred during the treatment period. This analysis is necessary to assess the signal of a serious risk, decreased survival with the concomitant use of panitumumab (Vectibix) and chemotherapy. The final report submission will include the primary datasets and programs used for generation of analyses; analyses will include, but may not be limited to, the analyses described in the statistical analysis plan.

The timetable you submitted on April 22, 2008 and June 16, 2008 states that you will conduct this trial according to the following timetable:

Protocol Submission:	November 28, 2007 [completed]
Clinical Trial Start Date:	March 9, 2006 [completed]
Projected Completion of Patient Accrual:	February 1, 2008 [completed]
Projected Completion of Clinical Trial:	September 30, 2009
Final Report Submission:	March 31, 2010

Submit the final study reports to your biologics license application (BLA), STN BL 125147. Submit chemistry, manufacturing, and controls protocols and all final reports to your BLA STN BL 125147. Use the following designators to prominently label all submissions, including supplements, relating to these postmarketing clinical trials as appropriate:

- **Required Postmarketing Protocol under 505(o)**
- **Required Postmarketing Final Report under 505(o)**
- **Required Postmarketing Correspondence under 505(o)**
- **Required Annual Report on Postmarketing Studies/Trials**

You are required to report periodically to FDA on the status of this clinical trial pursuant to sections 505(o)(3)(E)(ii) and 506B of the FDCA, as well as 21 CFR 601.70. Under section 505(o)(3)(E)(ii), you are also required to periodically report to FDA on the status of any study or trial otherwise undertaken to investigate a safety issue associated with Vectibix.

ORDER REQUIRING CASE REPORT FORM SUBMISSION UNDER 505(k)

Section 505(k)(1) of the FDCA authorizes FDA to order an applicant to provide certain reports to us if we find that such reports are necessary to determine whether there may be grounds for invoking section 505(e) of the FDCA. We have determined that the Case Report Forms described below are necessary for us to determine whether Vectibix is no longer safe under the conditions of use upon which it was approved.

Accordingly, under 505(k) you are ordered to provide the clinical trial Case Report Forms for Study 20040249: First-line treatment: entitled, "A Randomized, Open-label, Controlled, Clinical Trial of Chemotherapy and Bevacizumab With and Without Panitumumab in the First-line Treatment of Subjects With Metastatic Colorectal Cancer" for all patients who died while on Study 20040249 (within 30 days of the last dose of Vectibix) or who prematurely discontinued study treatment on Study 20040249 due to toxicity. We recommend that you submit this by June 30, 2008. If you propose an alternative timeline please provide a justification for the selected date.

POSTMARKETING COMMITMENT STUDIES SUBJECT TO REPORTING REQUIREMENTS OF 21 CFR 601.70.

We acknowledge your written commitment to provide additional information on an ongoing study as described in your correspondences of April 22, 2008 and June 16, 2008 as outlined below:

3. To provide a study report containing a final analysis of any significant toxicities that have occurred during the treatment period for study 20050181 entitled, "A Randomized, Multicenter Phase 3 Study to Compare the Efficacy of Panitumumab in Combination with Chemotherapy to the Efficacy of Chemotherapy Alone in Patients with Previously Treated Metastatic Colorectal Cancer." The final report submission will include the primary datasets and programs used for the generation of analyses; analyses will include, but may not be limited to, the analyses described in the statistical analysis plan.

Final Protocol Submission:	March 9, 2006 [completed]
Trial Start:	March 17, 2006 [completed]
Projected completion of patient accrual:	March 13, 2008 [completed]
Projected trial completion date:	September 30, 2009
Projected final trial report due date:	March 31, 2010

Submit all final report(s) to your BLA, STN 125147. Use the following designators to prominently label all submissions, including supplements, relating to this postmarketing clinical trial commitment as appropriate:

- Postmarketing Commitment Protocol
- Postmarketing Commitment - Final Report
- Postmarketing Correspondence
- Annual Status Report of Postmarketing Commitments

For each postmarketing study subject to the reporting requirements of 21 CFR 601.70, you must describe the status in an annual report on postmarketing studies for this product. The status report for each study should include:

- information to identify and describe the postmarketing commitment,
- the original schedule for the commitment,
- the status of the commitment (i.e. pending, ongoing, delayed, terminated, or submitted),
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment), and
- a revised schedule if the study schedule has changed and an explanation of the basis for the revision.

As described in 21 CFR 601.70(e), we may publicly disclose information regarding these postmarketing studies on our Web site (http://www.fda.gov/cder/pmc/default.htm). Please refer to the February 2006 Guidance for Industry: Reports on the Status of Postmarketing Study Commitments - Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see http://www.fda.gov/cder/guidance/5569fnl.htm) for further information.

CONTENT OF LABELING

Within 21 days of the date of this letter, 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, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "Product Correspondence – Final SPL for approved STN BL 125147/26." In addition, within 21 days of the date of this letter, amend any pending supplement(s) for this BLA with content of labeling in SPL format to include the changes approved in this supplement.

PROMOTIONAL MATERIALS

For products approved under Subpart E, sponsors are required to submit promotional materials 30 days before intended dissemination (21 CFR 601.45).

You may submit draft copies of the proposed introductory advertising and promotional labeling with a cover letter requesting advisory comments to the Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising and Communication, 5901-B Ammendale Road, Beltsville, MD 20705-1266. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by a FDA Form 2253.

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence to support that claim.

Please refer to http://www.fda.gov/cder/biologics/default.htm for important information regarding therapeutic biological products, including the addresses for submissions.

This information will be included in your biologics license application file. If you have any questions, please contact Melanie Pierce, Regulatory Project Manager, at 301-796-2320.

Sincerely,

Patricia Keegan

Patricia Keegan, M.D.
Director
Division of Biologic Oncology Products
Office of Oncology Drug Products
Center for Drug Evaluation and Research

Enclosure: Labeling