DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Our STN: BL 125084/103

OCT 0 2 2007

ImClone Systems, Incorporated
Attention: Cheryl Anderson
Vice President, Regulatory Affairs
33 ImClone Drive
Branchburg, NJ 08876

Dear Ms. Anderson:

Your request to supplement your biologics license application for cetuximab to expand the colorectal cancer indication to include cetuximab as a single agent in patients with EGFR-expressing, metastatic colorectal cancer after failure of both irinotecan- and oxaliplatin-based regimens, has been approved.

We approved your biologic license application for the use of cetuximab monotherapy for the treatment of EGFR-expressing, metastatic colorectal carcinoma in patients who are intolerant to irinotecan-based chemotherapy, under the regulations of 21 CFR 601 Subpart E for accelerated approval of biological products for serious or life-threatening illnesses. The data provided in this supplement verify the clinical benefit of cetuximab as monotherapy.

Please note that you have not verified the clinical benefit of cetuximab in combination with chemotherapy. Specifically, your approval for cetuximab, in combination with irinotecan, for treatment of EGFR-expressing, metastatic colorectal carcinoma in patients who are refractory to irinotecan-based chemotherapy, which was also approved under the regulations of 21 CFR 601 Subpart E, requires verification of clinical benefit, either through data to be submitted to BL STN 125084/115 or through additional studies.

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

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 deferring submission of your pediatric studies until December 31, 2007.

We acknowledge your written commitments as described in your letters of September 25 and 28, 2007, as outlined below:

Postmarketing Study Commitments subject to reporting requirements of 21 CFR 601.70.

1. To conduct a study to evaluate the impact of cetuximab on QTc as discussed in ICH E14. The protocol will be submitted by March 31, 2008, patient accrual will be completed by September 30, 2009, the study will be completed by January 29, 2010, and the final study report, including revised labeling, if applicable, will be submitted by June 30, 2010.

2. To submit data sets for primary study data, narrative summaries for all serious adverse events in both treatment arms, and a complete set of case report forms for all patients who died within 30 days of receiving study drug and all patients who discontinued treatment prematurely for study CA225006. These data should include determination of the secondary endpoints of progression-free survival and overall response rate. This information will be submitted as an amendment [redacted].

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 125084. Please use the following designators to label prominently all submissions, including supplements, relating to these postmarketing study commitments as appropriate:

- Postmarketing Study Commitment Protocol
- Postmarketing Study Commitment - Final Study Report
- Postmarketing Study Correspondence
- Annual Status Report of Postmarketing Study 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.

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 125084/103". 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.

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 information regarding therapeutic biological products, including the addresses for submissions.

This information will be included in your biologics license application file.

Sincerely,

Patricia Keegan

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