DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

Our STN: BL 125084/46

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

MAR 01 2006

Dear Ms. Anderson:

Your request to supplement your biologics license application for Cetuximab to include new indications, for use in combination with radiation therapy, for the treatment of locally or regionally advanced squamous cell carcinoma of the head and neck (SCCHN), and for use as a single agent for the treatment of patients with recurrent or metastatic SCCHN for whom prior platinum-based therapy has failed, has been approved.

We acknowledge your written commitments to provide additional information on ongoing studies as described in your letter of February 28, 2006, as outlined below:

Postmarketing studies subject to reporting requirements of 21 CFR 601.70.

1. To submit, for a period of five years, annual safety summaries assessing all reported fatal cases of myocardial infarction, congestive heart failure and/or arrhythmias as well as unexplained cases of sudden death observed in ImClone-sponsored or -supported trials of Erbitux, and in literature reports, and spontaneous safety reporting. Each of the summaries will be accompanied by case narratives. Each annual safety summary must contain cumulative information from the preceding year(s). These reports will be submitted annually by April 11th of each year. The first report will be submitted to STN 125084 by April 11, 2007, and identified as a Postmarketing Study Correspondence. The second, third, and forth reports should also be identified as Postmarketing Study Correspondence. The final summary report will be submitted to STN 125084 by April 11, 2011, and should be identified as a Postmarketing Study Final Report for this postmarketing commitment.

2. To submit by May 31, 2007, an interim analysis of early deaths by study arm, for the first 80 patients enrolled in study RTOG 0522 "A Randomized Phase III Trial of Concurrent Accelerated Radiation and Cisplatin versus Concurrent Accelerated Radiation, Cisplatin, and Cetuximab (C225) [Followed by Surgery for Selected Patients] For Stage III and IV Head and Neck Carcinomas". Accrual of the first 80 patients into RTOG-0522 is projected to be completed by November 30, 2006, and the total projected patient accrual of 720 patients completed by June 30, 2010.

3. To submit by March 31, 2011, the final study report for study RTOG-0522.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 125084. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your 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 Protocol
- Postmarketing Study Final Report
- Postmarketing Study Correspondence
- Annual Report on Postmarketing Studies

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 April 2001 Draft Guidance for Industry: Reports on the Status of Postmarketing Studies – Implementation of Section 130 of the Food and Drug Administration Modernization Act of 1997 (see http://www.fda.gov/cber/gdlns/post040401.htm) for further information.

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide SPL and PDF-format electronic copies as well as original paper copies (ten for circulars and five for other labels). In addition, you may wish to 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.

Effective August 29, 2005, the new address for all submissions to this application is:

Food and Drug Administration
Center for Drug Evaluation and Research
Therapeutic Biological Products Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

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

Attachment: Final Draft Labeling

CONCURRENCE PAGE

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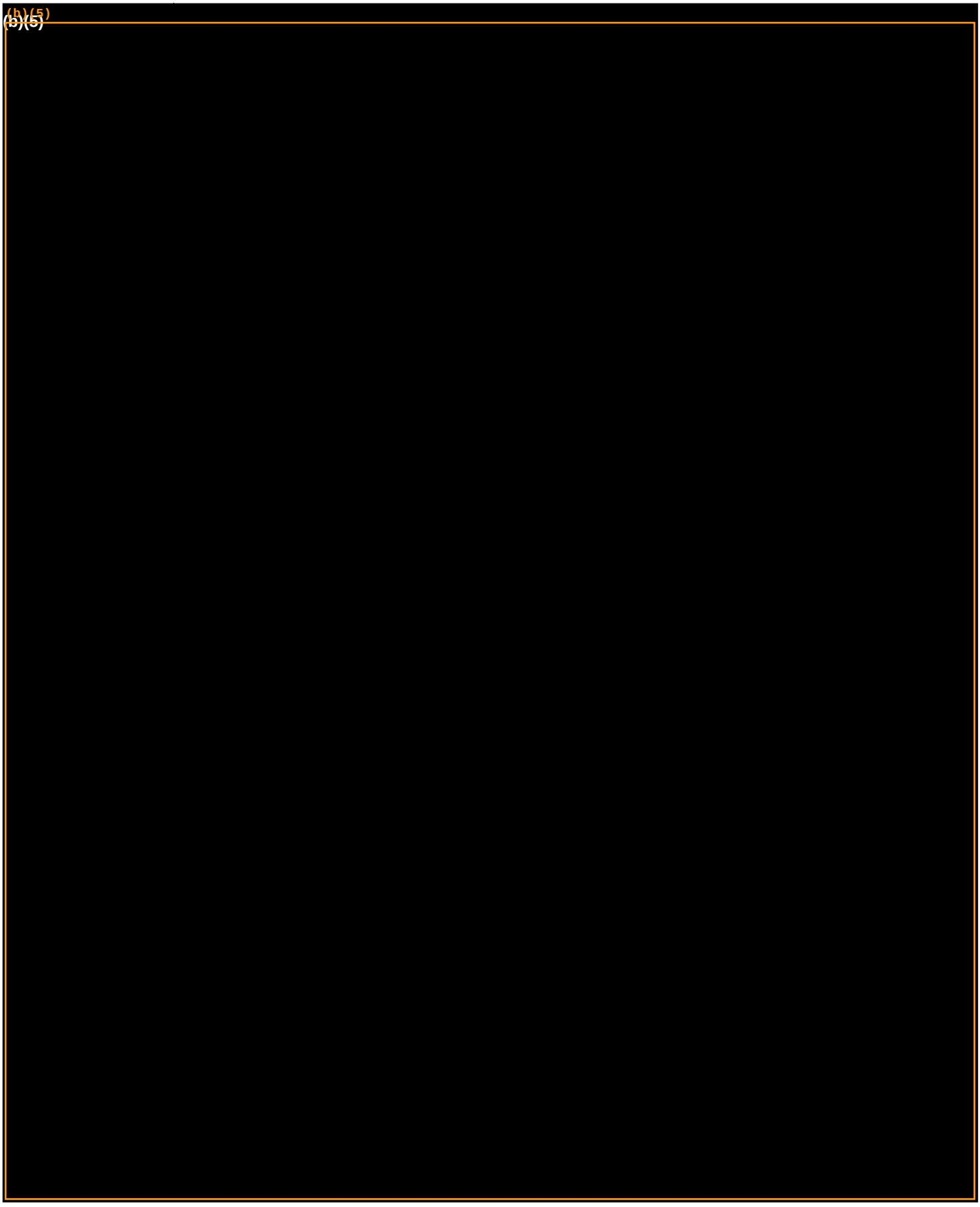

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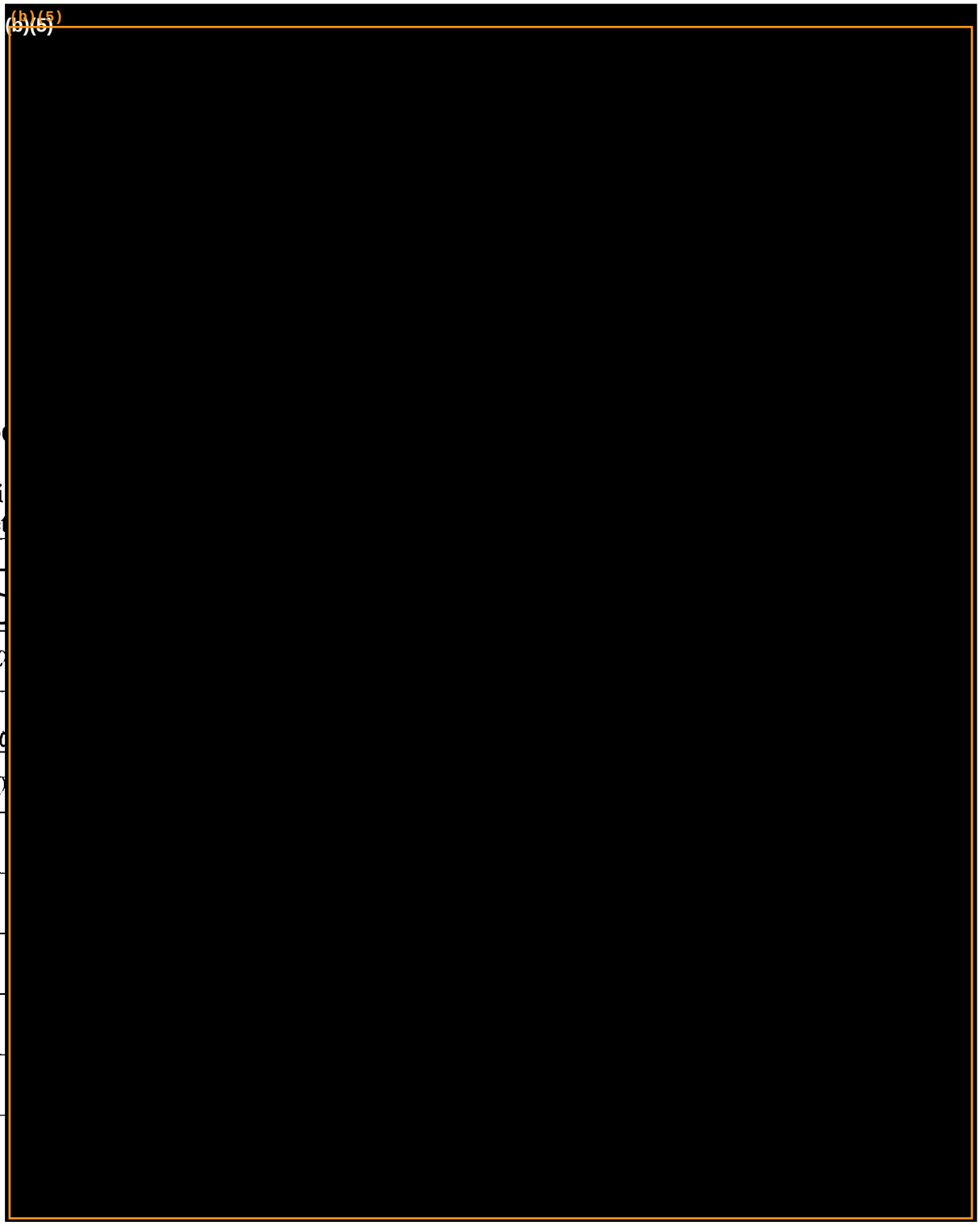

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