DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

JUL 30 2004

Our STN: BL 125057/16

Abbott Laboratories
Attention: James Steck, R.Ph.
Director, Global Pharmaceutical Regulatory Affairs
200 Abbott Park Road, D-491, AP30-1E
Abbott Park, IL 60064-6157

Dear Mr. Steck:

Your request to supplement your biologics license application for Adalimumab to expand the indication to include improving physical function in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more DMARDS has been approved.

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 for ages four to seventeen years until March 31, 2006. We are also deferring the submission of your pediatric studies for ages zero to less than four years until March 31, 2007.

**Postmarketing Studies subject to reporting requirements of 21 CFR 601.70.**

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The statuses of these postmarketing studies shall be reported annually according to 21 CFR 601.70. These commitments are listed below.

1. To continue study DE038, "A Multi-center, Randomized, Double-Blind, Placebo-Controlled Study of the Safety and Efficacy of Human Anti-TNF Monoclonal Antibody Adalimumab in Children With Polyarticular Juvenile Rheumatoid Arthritis" which is currently ongoing. The protocol was filed to (b)(4) June 28, 2002, and the study was initiated on September 13, 2002. Enrollment will be completed by March 31, 2004, and study completion will occur by March 31, 2005. The final study report will be submitted by March 31, 2006. Please note that this revises the schedule for PMC #5 in our approval letter of December 31, 2002 letter.

2. To evaluate the feasibility of conducting a study in patients age zero to less than 4 years, and if appropriate, submit a pediatric study plan or request a waiver by March 31, 2007.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 125057. Submit all study final reports to your BLA, STN BL 125057. For administrative purposes, all submissions related to these pediatric postmarketing study commitments must be clearly designated "Required Pediatric Study Commitments". In addition, 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), and
- an explanation of the status including, for clinical studies, the patient accrual rate (i.e. number enrolled to date and the total planned enrollment).

As described in 21 CFR 601.70(e), we may publically 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.

Pursuant to 21 CFR 201.57(f)(2), patient labeling must be reprinted at the end of the package insert. We request that the text of information distributed to patients be printed in a minimum of 10 point font.

Please submit all final printed labeling at the time of use and include implementation information on FDA Form 356h. Please provide a PDF-format electronic copy 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 Division of Drug Marketing, Advertising and Communication (HFD-42), Center for Drug Evaluation and Research, 5600 Fishers Lane/Room 8B45, Rockville, MD 20857. Final printed advertising and promotional labeling should be submitted at the time of initial dissemination, accompanied by an 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.

The regulatory responsibility for review and continuing oversight for this product transferred from the Center for Biologics Evaluation and Research to the Center for Drug Evaluation and Research effective June 30, 2003. For further information about the transfer, please see http://www.fda.gov/cder/biologics/default.htm. Until further notice, however, all correspondence, except as provided elsewhere in this letter, should continue to be addressed to:

CBER Document Control Center
Attn: Office of Therapeutics Research and Review
Suite 200N (HFM-99)
1401 Rockville Pike
Rockville, Maryland 20852-1448

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

Sincerely,

(b)(6)

Marc Walton, M.D., Ph.D.
Director
Division of Therapeutic Biological Internal Medicine Products
Office of Drug Evaluation VI
Center for Drug Evaluation and Research

## CONCURRENCE PAGE

Letter Type: LETTER: Approval (AP)

Summary Text: Clinical Supplmt. Efficacy - New/Expanded Indication
**REVIEW COMPLETION REQUIRED BY: RIS**

**SS Data Check:**

- **Place copy of Approval Ltr. with original signature concurrence page in Archival package behind the "Approval Materials" Tab after LAR (Licensing Action Recommendation).**

**RIS Data Check:**

- **Verify short summary – Ltr. & Submission screen should match.**
- **Check Letter for PMCs (if PMCs – add "PMCs – Approved With" special characteristic code.)**
- **Check if Major Approval – if so – add code.**
- **Perform Review Completion Process**
- **Milestone: Confirm Approved Status**

cc: S. Kozlowski, HFM-555
M. Walton, HFM-576
P. Swann, HFM-555
DARP BLA file, HFM-585
K. Weiss, HFM-500
B. Conner, HFM-588
J. Siegel, HFM- 582
L. Liang, HFM-582
M. Kiester, DDMAC, HFD-42
Catherine Miller, HFD-[redacted] 42
Jeanne Best, HFD - 410
Hyon Kwon, HFD-430
L. Martynec, HFM- 573
Bo-Guang Zhen, HFM- 711
J. Lloyd Johnson, HFD- 46
Grace Carmouze, HFD-960
Terrie Crescenzi, HFD-960
B. Duvall-Miller, HFD-020
C. Lee, HFM-570
IPCB, HFD-322
HFD-240/B. Poole
HFD-013/D. Taub, (ORP/DIDP w/revised labeling)
HFD-O13/H. Brubaker, (ORP/DIDP w/revised labeling)
Mary Dempsey, OPSS, HFD-400
P. Guinn, OEP, HFD-006

History: B. Conner 7.28.04:1.29.04: T. Pagan-Motta: 7.29.04

File Name: (S:\Conner\BLA\Letters\125057_16

(b)(6)

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