CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

sBLA 125057/110

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

JAN 18 2008

Our STN: BL 125057/110

Abbott Laboratories
Attention: Meg Drew, M.P.H.
Associate Director, Immunology Development
Global Pharmaceutical Regulatory Affairs
Dept. PA72, Bldg. AP34-3
200 Abbott Park Road
Abbott Park, IL 60064-6188

Dear Ms. Drew:

Your request to supplement your biologics license application for Humira® (adalimumab) 40 mg, to include a new indication for the treatment of adult patients with moderate to severe chronic plaque psoriasis who are candidates for systemic therapy or phototherapy, and when other systemic therapies are medically less appropriate, has been approved.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the 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 to the enclosed labeling (text for the package insert and Medication Guide). 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 125057/110". In addition, within 14 days of the date of this letter, amend any pending supplements for this BLA with content of labeling in SPL format to include the changes approved in this supplement.

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your January 3, 2008 submission containing final printed carton labels.

PEDIATRIC RESEARCH EQUITY ACT (PREA)

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 ages 0 up to 4 years because studies are impossible or highly impractical due to the small number of patients and the disease may be difficult to accurately diagnose. We are deferring submission of your pediatric studies for ages 4 to 17 years for this application because discussion and design of pediatric studies should be delayed until additional safety data have been collected and reviewed.

1. Your deferred pediatric study required by section 505B(a) of the Food, Drug, and Cosmetic Act is a required postmarketing study commitment. The status of this postmarketing study must be reported annually according to 21 CFR 601.70 and section 505B(a)(3)(B) of the Food, Drug, and Cosmetic Act. This commitment is listed below.

   Deferred pediatric study under PREA for the treatment of moderate to severe chronic plaque psoriasis in pediatric patients ages 4 to 17. The pediatric plan is to assess data anticipated from ongoing trials as well as further analysis and assessment of data, including data pertaining to the diagnosis and treatment of psoriasis in the pediatric population, and to establish a study plan that incorporates this new data.

   Pediatric plan proposal due: January 2013

   Submit final study reports to this BLA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated **"Required Pediatric Study Commitments"**.

POSTMARKETING COMMITMENTS

We remind you of your written commitments to provide additional information on ongoing studies and to conduct postmarketing studies as described in your submission dated January 16, 2008. These commitments are listed below.

2. Conduct a prospective, multi-center registry including 5000 adult psoriasis patients treated with Humira in the United States. This registry will characterize and assess the incidence of serious adverse events (including serious infections, tuberculosis, opportunistic infections, malignancies, hypersensitivity reactions, autoimmune reactions and deaths) as well as other adverse events of interest in the study cohort. All enrolled study patients will be evaluated for a period of at least 10 years with comprehensive annual reports provided to the Agency. Collect data on the patient characteristics, demographics and drug exposure (including dose, duration and time to onset of adverse event). The collection of data will be via active surveillance methods and data will be validated by a review of medical records as per the guidance for industry titled *Good Pharmacovigilance Practices and Pharmacoepidemiologic Assessment.*

Final study protocol submitted:	March 2008
Patient accrual initiated:	September 2008
Progress Reports:	Annually starting February 2009
Interim Reports:	Every other year starting February 2010

Study Completion: October 2022
Final Report Submission: January 2023

The final study protocol will incorporate the design methods agreed upon in your submissions up to and including December 26, 2007 and any revisions recommended by the Agency in subsequent communication.

3. Submit the final study report for trial M03-658, "A Multicenter Open-Label Continuation Study in Moderate to Severe Chronic Plaque Psoriasis Subjects who Completed a Preceding Psoriasis Clinical Study with Adalimumab".

Final Report Submission: April 2010

4. Provide information on effects of discontinuation of Humira followed by a second course of Humira in patients treated successfully with the drug.

This information will be obtained from a minimum of 120 evaluable subjects currently participating in Study M03-658 "A Multicenter Open-Label Continuation Study in Moderate to Severe Chronic Plaque Psoriasis Subjects who Completed a Preceding Psoriasis Clinical Study with Adalimumab". Subjects meeting response criteria will be discontinued from treatment and reinitiated Humira therapy upon relapse to evaluate whether additional use of Humira will impact safety and efficacy.

Study Report Submission April 2010

If the information from ongoing clinical trials is insufficient, a new trial will be conducted to assess effects of discontinuation followed by a second course of Humira in patients treated successfully with the drug.

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 nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to your BLA STN BL 125057. 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.

MEDICATION GUIDE

We determined that Humira poses a serious and significant public health concern relating to increased risk for serious infections. This concern required development of a Medication Guide under 21 CFR 208 in order to prevent serious adverse effects, inform patients of information concerning risks that could affect their decision to use or continue to use the drug, and/or assure effective use of the drug.
Please note that:

- this Medication Guide must be printed immediately following the last section of labeling or, alternatively, accompany the prescription drug labeling [21 CFR 201.57(c)(18)] or 21 CFR 201.80(f)(2)];

- you are responsible for ensuring that this Medication Guide is available for distribution to every patient who is dispensed a prescription for this product [21 CFR 208.24]; and

- the final printed Medication Guide distributed to patients must conform to all conditions described in 21 CFR 208.20, including a minimum of 10 point text.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and 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 promotional labeling, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this BLA and to the following address:

MedWatch
Food and Drug Administration
HFD-001, Suite 5100
5515 Security Lane
Rockville, MD 20852

REPORTING REQUIREMENTS

You must submit adverse experience reports under the adverse experience reporting requirements for licensed biological products (21 CFR 600.80). You should submit postmarketing adverse experience reports to the following address:

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

Prominently identify all adverse experience reports as described in 21 CFR 60.80.

You must submit distribution reports under the distribution reporting requirements for licensed biological products (21 CFR 600.81).

You must submit reports of biological product deviations under 21 CFR 600.14. You should promptly identify and investigate all manufacturing deviations, including those associated with processing, testing, packing, labeling, storage, holding and distribution. If the deviation involves a distributed product, may affect the safety, purity, or potency of the product, and meets the other criteria in the regulation, you must submit a report on Form FDA-3486 to the following address:

Division of Compliance Risk Management and Surveillance
(HFD-330) Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Biological product deviations sent by courier or overnight mail should be addressed to:

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Compliance
Division of Compliance Risk Management and Surveillance
(HFD-330) Montrose Metro 2
11919 Rockville Pike
Rockville, MD 20852

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.

If you have any questions, call Tamika White, Regulatory Project Manager, at (301) 796-0310.

Sincerely,

Susan J. Walker, M.D., F.A.A.D.
Director
Division of Dermatology and Dental Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

Enclosure