DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20852

Our STN: BL 103772/5138

MAY 19 2006

Centocor, Inc.
Attention: Stella S. Jones, Ph.D.
Vice President, Worldwide Regulatory Affairs
200 Great Valley Parkway
Malvern, PA 19355-1307

Dear Dr. Jones:

Your request to supplement your biologics license application for Infliximab to include a new indication for reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy, has been approved.

This fulfills your commitment to conduct a clinical trial in pediatric patients with Crohn's disease to determine the consistency of benefits with those observed in adults, as stated in commitment number one of the August 24, 1998, approval letter.

We acknowledge your agreement to provide additional information and to conduct postmarketing studies as described in your commitment letter of May 18, 2006, and as outlined below:

Postmarketing Studies subject to reporting requirements of 21 CFR 601.70.

1. Centocor commits to designing and implementing a registry of patients with pediatric Crohn's disease being treated with REMICADE that will be established to obtain long-term clinical status and safety information. Information will be collected on patient demographics, disease characteristics, history of concomitant medications, dose and duration and frequency of REMICADE administration, clinical status, adverse events including dysplasias and malignancies of all types, infections, autoimmune disease, assessment of immunogenicity, and potential effects of antibody formation. The age range should include patients ages 0 to 19 years.

   This registry will be designed so that detailed clinical status information is collected at registry entry and on a 6 month basis for at least 20 years. Centocor commits to expand the currently existing Pediatric IBD Registry, and will actively encourage both patients and physicians to participate in the registry through an advertisement campaign, that includes a plan for proactive communication of associated risk. Centocor also commits to recruiting at least 2,000 REMICADE treated pediatric Crohn's patients, which will provide an adequate number of patients to participate in the registry so that outcome measures will be collected

communication for serious adverse events that are reported through the registry. The registry data will be analyzed at yearly intervals and the results will be submitted in annual reports for BB-IND 5389. A study protocol will be submitted to CDER by September 30, 2006, for FDA concurrence, and the study will be implemented by December 31, 2006. The final study report under this registry will be submitted to CDER by June 30, 2027.

We request that you submit clinical protocols to your IND, with a cross-reference letter to this biologics license application (BLA), STN BL 103772. 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.

Pursuant to 21 CFR 201.57(f)(2), patient labeling must be reprinted at the end of the package insert.

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 Food and Drug Administration, Center for Drug Evaluation and Research, Division of Drug Marketing, Advertising and Communication, 5901-B

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,

Brian E. Harvey, M.D., Ph.D.
Director
Division of Gastroenterology Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

CDER-OCTAP960PM (PEDs e-mail account)
HFD-322/IPCB/ E. Rivera-Martinez
HFD-430/ODS/DDRE (hard copy)
HFD-410/CDER Medwatch Safety Labeling (hard copy)

History: CLStark:5.16.2006:M. Swider:5.17.2006

File Name: N:\Stark\Centocor\STN 103772_5138\STN 103772_5138 approval letter.doc

Office	Name/Signature	Date
DGP	Bruce Strongin	5-18-06
DGP		5/18/2006
DGP	John E Hyde	5-19-06
DGP	Brian E. Harvey	5/19/06

CONCURRENCE PAGE

Letter Type: LETTER: Approval (AP)
LETTER: Fulfillment of PMC (FPC) [ADD ONLY IF FULFILLING A PMC]
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: Attached label is sent to everyone
HFD-180/L. Liang
HFD-180/J. Hyde
HFD-180/J. Korvick
HFD-180/B. Harvey
HFD-180/M. Swider
HFD-180/B. Strongin
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HFD-240/OTCOM/ B. Poole
HFI-20/Press/ L. Gelb
HFI-20/Press/ J. Brodsky
HFD-230/OTCOM/CDER WebMaster
HFD-001/B. Duvall-Miller (if PMC commitments)
HFD-109/C. O'Leary
HFD-42/DDMAC/J. Wang
HFD-410/ODS/DSRCS/ Karen Young