DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-722/S-008
NDA 50-723/S-006
NDA 50-758/S-005
NDA 50-759/S-008

Hoffmann-La Roche, Inc.
Attention: Anthony Corrado, Program Director, Drug Regulatory Affairs
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Mr. Corrado:

Please refer to your supplemental new drug applications listed below, which were submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act:

NDA #	Drug Product	Supplement number	Letter Date	Receipt Date
50-722	CellCept® (mycophenolate mofetil) Capsules	S-008	March 14, 2001	March 15, 2001
50-723	CellCept® (mycophenolate mofetil) Tablets	S-006	March 14, 2001	March 15, 2001
50-758	CellCept® (mycophenolate mofetil) Intravenous	S-005	March 14, 2001	March 15, 2001
50-759	CellCept® (mycophenolate mofetil) Oral Suspension	S-008	March 14, 2001	March 15, 2001

We acknowledge receipt of your submissions dated March 16, October 15, and November 5, 2001, and March 21, 2002.

These "Changes Being Effected" supplemental new drug applications provide for the following revisions to the package insert:

- The cut-off value for a table of adverse events (AEs) that occurred in the CellCept® group of controlled studies for the prevention of renal, cardiac, and hepatic allograft rejection was raised from 10% to 20%.

- In this context, all of the AEs that were deleted from the previous table were added to another, which reports events in 3 to < 20% of patients treated with CellCept®, cyclosporine, and corticosteroids. In addition, these AEs are no longer organized by organ.
- The following statement was added to the **PRECAUTIONS/*Drug Interactions***/*Live Vaccines* subsection: "Influenza vaccination may be of value. Prescribers should refer to national guidelines for influenza vaccination."
- The following changes were made to the **ADVERSE REACTIONS/*CellCept Oral*** subsection (additions are indicated by a double underline and deletions are struck out):

  "~~However, the following adverse events were reported in the placebo-controlled renal transplant study but not reported in the azathioprine-controlled renal transplant studies with an incidence of ≥10% urinary tract disorder, bronchitis, and pneumonia.~~"

  "Patients receiving CellCept alone or as part of an immunosuppressive regimen are at increased risk of developing lymphomas and other malignancies, particularly of the skin (see **WARNINGS**)."

  "All transplant patients are at increased risk of opportunistic infections. The risk increases with total immunosuppressive load (see **WARNINGS**)."

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert submitted November 5, 2001).

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please mount individually ten of the copies on heavyweight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDAs (January 1999). For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 50-722/S-008, NDA 50-723/S-006, NDA 50-758/S-005, and NDA 50-759/S-008." Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about these drugs products (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Matthew A. Bacho, Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and
Immunologic Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Renata Albrecht
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