DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-083/S-030
NDA 21-110/S-038

Wyeth Pharmaceuticals, Inc.
Attention: David K. Ellis, Ph.D.
Assistant Vice President, Global Regulatory Affairs
P.O. Box 8299
Philadelphia, PA 19101-8299

Dear Dr. Ellis:

Please refer to your New Drug Applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NDA Number	Name of Drug Product	Supplement Number	Date of Supplement	Date of Receipt
21-083	Rapamune® (sirolimus) Oral Solution, 1 mg/mL	S-030	July 13, 2006	July 14, 2006
21-110	Rapamune® (sirolimus) Tablets, 1 mg, 2 mg, and 5 mg	S-038	July 13, 2006	July 14, 2006

We acknowledge receipt of your submissions dated January 10, 2007.

These supplemental applications, submitted as "Changes Being Effected", provide for the addition of a new subsection in **PRECAUTIONS** section**,** before the ***Calcineurin inhibitor-induced hemolytic uremic syndrome*** subsection of the package insert as follows (underlined text indicates addition):

> ***De Novo Use Without Cyclosporine***
>
> The safety and efficacy of *de novo* use of Rapamune without cyclosporine is not established in renal transplant patients. In a multi-center clinical study, *de novo* renal transplant patients treated with Rapamune, MMF, steroids, and an IL-2 receptor antagonist had significantly higher acute rejection rates and numerically higher death rates compared to patients treated with cyclosporine, MMF, steroids, and IL-2 receptor antagonist. A benefit, in terms of better renal function, was not apparent in the treatment arm with *de novo* use of Rapamune without cyclosporine. These findings were also observed in a similar treatment group of another clinical trial.

We have completed our review of these applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

Submit revised content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html, that is identical in content to the enclosed labeling text. Upon receipt and verification, we will transmit that version to the National Library of Medicine for posting on the DailyMed website.

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

MEDWATCH
Food and Drug Administration
WO 22, Room 4447
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Hyun J. Son, Pharm.D., Regulatory Project Manager, at (301) 796-1600.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Package Insert

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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