DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-083/S-038
NDA 21-110/S-049

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 supplemental new drug applications dated and received on July 29, 2008, 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	S-038	July 29, 2008	July 29, 2008
21-110	Rapamune® (sirolimus) Tablets	S-049	July 29, 2008	July 29, 2008

These "Changes Being Effected" supplemental new drug applications provides for the following changes to the package insert, as well as various editorial changes not described in this letter (additions are noted by underline and deletions are noted by ~~strikethrough~~):

1. In the **6 ADVERSE REACTIONS/6.6 Postmarketing Experience** subsection the ***Respiratory*** bullet is modified as follows:

> ***Respiratory*** – Cases of interstitial lung disease (including pneumonitis, bronchiolitis obliterans organizing pneumonia [BOOP], and pulmonary fibrosis), some fatal, with no identified infectious etiology have occurred in patients receiving immunosuppressive regimens including Rapamune. In some cases, the interstitial lung disease has resolved upon discontinuation or dose reduction of Rapamune. The risk may be increased as the sirolimus trough concentration increases [see *Warnings and Precautions (5.10)*]; pulmonary hemorrhage; pleural effusion; alveolar proteinosis.

2. In the **6 ADVERSE REACTIONS/6.6 Postmarketing Experience** subsection the ***Urogenital*** bullet is modified as follows:

> ***Urogenital***– Nephrotic syndrome, proteinuria, focal segmental glomerulosclerosis. Azoospermia has been reported with the use of Rapamune and has been reversible upon discontinuation of Rapamune in most cases.

We 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.

The final printed labeling (FPL) must be identical to the enclosed labeling patient package insert submitted July 29, 2008.

As soon as possible, please submit the 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 to the enclosed labeling (text for the package insert). Upon receipt, we will transmit this version to the National Library of Medicine for public dissemination. For administrative purposes, please designate these submissions, "**SPL for approved NDA 21-083/S-038 and NDA 21-110/S-049**."

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 this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

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 Sherry Spriggs, Regulatory Project Manager, at (301) 796-4018.

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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