DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-083/S-020, S-021
NDA 21-110/S-027, S-028

Wyeth Pharmaceuticals, Inc.
Attention: Dr. David K. Ellis, Ph.D.
Senior Director
Worldwide Regulatory Affairs
Box 8299
Philadelphia, PA 19101-8299

Dear Dr. Ellis:

Please refer to your supplemental new drug applications dated January 13, 2005, received January 14, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for:

NDA #	Drug Product	Supplement number
21-083	Rapamune® (sirolimus) Oral Solution, 1 mg/mL	S-020
21-110	Rapamune® (sirolimus) Tablets, 1 mg, 2 mg	S-027

We acknowledge receipt of your submission dated June 22, 2005.

These "Prior Approval" supplemental new drug applications provide for the following revision to the package insert (addition is double underlined):

- In **PRECAUTIONS/Drug Interactions/*Drugs which may be coadministered without dose adjustment,*** the following statement concerning atorvastatin was added:

  Atorvastatin: Atorvastatin, 20 mg, was given daily for 10 days to 23 healthy volunteers, followed by a combined regimen of sirolimus oral solution, 2 mg, and atorvastatin, 20 mg, for 5 days.

Please also refer to your supplemental new drug applications dated January 18, 2005, received January 19, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for:

NDA #	Drug Product	Supplement number
21-083	Rapamune® (sirolimus) Oral Solution, 1 mg/mL	S-021
21-110	Rapamune® (sirolimus) Tablets, 1 mg, 2 mg	S-028

We acknowledge receipt of your submissions dated June 1, 2005 and June 22, 2005.

These "Changes Being Effected" supplemental new drug applications provide for the following revision to the package insert (addition is double underlined):

- The following statement was added under **DOSAGE AND ADMINISTRATION/Instructions for Dilution and Administration of Rapamune® Oral Solution:**

  Rapamune Oral Solution contains polysorbate-80, which is known to increase the rate of di-(2-ethylhexyl)phthalate (DEHP) extraction from polyvinyl chloride (PVC). This should be considered during the preparation and administration of Rapamune Oral Solution. It is important that the recommendations in **DOSAGE AND ADMINISTRATION** be followed closely.

We have completed the review of these supplemental new drug applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text (enclosed). Accordingly, these supplemental applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (text for the package insert submitted June 22, 2005).

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submission in Electronic Format – NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate these submissions as "**FPL for approved supplements NDA 21-083/S-020, S-021 and NDA 21-110/S-027, S-028".** Approval of these submissions by FDA is not required before the labeling is used.

If a letter communicating important information about these drug 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 these NDAs 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 Rebecca Saville, Pharm.D., Project Manager at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Renata Albrecht, M.D.
Director
Division of Special Pathogen and
Transplant 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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