DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-083/S-015
NDA 21-110/S-015

Wyeth Pharmaceuticals, Inc.
Attention: Tracy D. Rockney
Director
Worldwide Regulatory Affairs
Box 8299
Philadelphia, PA 19101-8299

Dear Ms. Rockney:

Please refer to your supplemental new drug applications dated April 25, 2003, received April 28, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act:

NDA Number	Drug Product	Supplement Number
21-083	Rapamune® (sirolimus) Oral Solution, 1 mg/mL	S-015
21-110	Rapamune® (sirolimus) Tablets, 1 mg, 2 mg	S-015

We acknowledge receipt of your submission dated July 8, 2003.

These "Changes Being Effected (CBE)" supplemental new drug applications provide for the following revisions to the package insert (additions are double underlined and deletions are strikethrough):

1. WARNINGS

- The following sentence was added after the first paragraph:

  "Hypersensitivity reactions, including anaphylactic/anaphylactoid reactions, have been associated with the administration of sirolimus (see **ADVERSE REACTIONS**)."

2. **ADVERSE REACTIONS**

- Venous thromboembolism was added to the CARDIOVASCULAR SYSTEM subsection to read:

"CARDIOVASCULAR SYSTEM: atrial fibrillation, congestive heart failure, hemorrhage, hypervolemia, hypotension, palpitation, peripheral vascular disorder, postural hypotension, syncope, tachycardia, thrombophlebitis, thrombosis, vasodilatation, venous thromboembolism;…"

- The OTHER CLINICAL EXPERIENCE subsection was revised to read:

"There have been reports of neutropenia and rare reports of pancytopenia. Hypersensitivity reactions, including anaphylactic/anaphylactoid reactions, have been associated with the administration of sirolimus (see **WARNINGS**)."

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 products are safe and effective for use as recommended in the final printed labeling submitted on July 8, 2003. Accordingly, these supplemental new drug applications are approved effective on the date of this letter.

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 Robin Anderson, Labeling Reviewer 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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