DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 50-715/S-025
NDA 50-716/S-026

Novartis Pharmaceuticals Corporation
Attention: Mr. Ronald G. Van Valen
Director, Drug Regulatory Affairs
One Health Plaza
East Hanover, NJ 07936-1080

Dear Mr. Van Valen:

We have received your supplemental new drug applications submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

NDA #	Name of Drug Product	Supplement Number	Date of Supplement	Date of Receipt
50-715	Neoral® Soft Gelatin Capsules (cyclosporine capsules, USP) MODIFIED, 25 mg and 100 mg	S-025	November 10, 2006	November 13, 2006
50-716	Neoral® Oral Solution (cyclosporine oral solution, USP) MODIFIED, 100 mg/mL	S-026	November 10, 2006	November 13, 2006

These supplemental new drug applications provide for revisions to the **WARNINGS**: **Kidney, Liver and Heart Transplant** and **PRECAUTIONS**: **Drug Interactions** subsections of the package insert to add new information obtained from post-marketing surveillance and literature reports.

The proposed revisions to the package insert are listed below (<u>double underlined</u> = added text):

1. The **WARNINGS**, **Kidney, Liver and Heart Transplant** subsection, the eighth paragraph after the Nephrotoxicity vs. Rejection table, was revised to read as follows:

   As in patients receiving other immunosuppressants, those patients receiving cyclosporine are at increased risk for development of lymphomas and other malignancies, particularly those of the skin. <u>Patients taking cyclosporine should be warned to avoid excess ultraviolet light exposure.</u> The increased risk appears related to the intensity and duration of immunosuppression rather than to the use of specific agents. Because of the danger of oversuppression of the immune system resulting in increased risk of infection or malignancy, a treatment regimen containing multiple immunosuppressants should be used with caution. <u>Transplant patients receiving cyclosporine are at increased risk for serious infection with fatal outcome.</u>

2. In the **PRECAUTIONS/Drug Interactions/*Drugs That May Potentiate Renal Dysfunction*** subsection, under the *Other Drugs* column, methotrexate is added.

3. In the **PRECAUTIONS/Drug Interactions/*Drugs That Increase Cyclosporine Concentrations*** subsection**,** under the *Antifungals* column, voriconazole is added.

4. In the **PRECAUTIONS/Drug Interactions/*Drugs/Dietary Supplements That Decrease Cyclosporine Concentrations*** subsection, under the *Other Drugs/Dietary Supplements* column, oxcarbazepine and bosentan are added.

We completed our review of these applications. 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 these drug products (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
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

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 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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