CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-266

21-267

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-266
NDA 21-267

Pfizer Inc.
Attention: Maureen Garvey, Ph.D.
Director, Worldwide Regulatory Affairs
235 East 42nd Street
New York, NY 10017

Dear Dr. Garvey:

Please refer to your new drug applications (NDAs) dated November 17, 2000, received November 17, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for VFEND™ (voriconazole) Tablets, NDA 21-266, and VFEND™ (voriconazole for infusion), NDA 21-267.

We acknowledge receipt of your submissions dated:

December 17, 2001 (2)	February 19, 2002	April 19, 2002
December 19, 2001	February 21, 2002	April 24, 2002
December 21, 2001	February 25, 2002 (2)	May 2, 2002 (2)
January 4, 2002	February 28, 2002	May 3, 2002
January 14, 2002	March 14, 2002	May 21, 2002
January 22, 2002	March 26, 2002	May 23, 2002 (2)
January 29, 2002	April 5, 2002	
January 31, 2002	April 8, 2002	

Your submission of March 26, 2002 constituted a complete response to our December 17, 2001 action letter.

These new drug applications provide for the use of VFEND™ (voriconazole) Tablets and VFEND™ (voriconazole for infusion) for the treatment of invasive aspergillosis and serious fungal infections caused by *Scedosporium apiospermum* and *Fusarium* spp., including *Fusarium solani*, in patients intolerant of, or refractory to, other therapy.

We have completed the review of these 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 agreed upon labeling text. Accordingly, these applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and submitted labeling (immediate container and carton labels submitted November 17, 2000). Marketing the products with FPL that is not identical to the approved labeling text may render the products misbranded and unapproved new drugs.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as they are available but no more than 30 days after they are printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated "FPL for approved NDA 21-266" and "FPL for approved NDA 21-267." Approval of these submissions by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitments in your submissions dated March 26, 2002 and May 23, 2002. These commitments are listed below.

1. Drug interaction study to evaluate the two-way interactions between voriconazole and methadone

Protocol Submission:	1Q2003
Study Start:	1Q2003
Final Report Submission:	1Q2004

2. Drug interaction study to evaluate the two-way interactions between voriconazole and representative HIV protease inhibitors (e.g., ritonavir)

Protocol Submission:	July 2002
Study Start:	August 2002
Final Report Submission:	August 2003

3. Drug interaction study to evaluate the two-way interactions between voriconazole and representative non-nucleoside reverse transcriptase inhibitors (e.g., efavirenz)

Protocol Submission:	October 2002
Study Start:	November 2002
Final Report Submission:	November 2003

4. Study to examine the effects of voriconazole on cardiac contractility in experimental animals or humans

Protocol Submission:	October 2002
Study Start:	January 2003
Final Report Submission:	1Q2003

Submit clinical protocols to your INDs for these products. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to these NDAs. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to these NDAs. The status summary should include expected study completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled **"Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."**

Additionally, we acknowledge that your submission of March 26, 2002 stated your intention to continue to collect additional information about voriconazole. We note that you will continue to assess the efficacy of voriconazole against the non-fumigatus species of *Aspergillus*. You will also continue to assess cross-resistance patterns between voriconazole, itraconazole and fluconazole from all *Candida*, *Aspergillus*, *Fusarium* and *Scedosporium* isolates, and continue to assess drug resistance development in patients infected with *Candida*, *Fusarium* and *Scedosporium* isolates.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (21 CFR 314.55).

Based on the information submitted, we conclude the following:

- For the treatment of invasive aspergillosis and serious fungal infections caused by *Scedosporium apiospermum* and *Fusarium* spp., including *Fusarium solani*, in patients intolerant of, or refractory to, other therapy, we are deferring submission of your pediatric studies until December 31, 2003.

In addition, please submit three copies of the introductory promotional materials that you propose to use for these products. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Special Pathogen and Immunologic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Please submit one market package of each of the drug products when it is available.

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, call Jouhayna Saliba, Regulatory Project Manager, at (301) 827-2127.

Sincerely,

{See appended electronic signature page}

Mark J. Goldberger, M.D., M.P.H.
Director
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure