DEPARTMENT OF HEALTH & HUMAN SERVICES **Public Health Service**

Food and Drug Administration
Rockville MD 20857

NDA 21-434

Pharmacia & Upjohn
Attention: Roma J. Thomas
Regulatory Affairs Manager
7000 Portage Road
Kalamazoo, Michigan 49001

Dear Ms.Thomas:

Please refer to your new drug application (NDA) dated December 26, 2001, received December 26, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for XANAX® XR (alprazolam) Extended-release Tablets.

We acknowledge receipt of your submissions dated November 20 and December 23, 2002.

The November 20, 2002, submission constituted a complete response to our action letter.

This new drug application provides for the use of Xanax® XR for the treatment of panic disorder.

We also refer to the January 15, 2003, telephone conversation between Ms. Roma Thomas, Pharmacia Regulatory Affairs Manager, and Ms. Anna Marie H. Weikel, Project Manager of this Division, during which the final labeling was agreed upon.

We have completed the review of this application, 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 enclosed labeling text. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the agreed upon enclosed labeling (text for the package insert and patient package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-434." Approval of this submission by FDA is not required before the labeling is used.

FDA's Pediatric Rule [at 21 CFR 314.55/21 CFR 601.27] was challenged in court. On October 17, 2002, the court ruled that FDA did not have the authority to issue the Pediatric Rule and has barred FDA from enforcing it. Although the government decided not to pursue an appeal in the courts, it will work with Congress in an effort to enact legislation requiring pharmaceutical manufacturers to conduct appropriate pediatric clinical trials. In addition, third party interveners have decided to appeal the court's decision striking down the rule. Therefore, we encourage you to submit a pediatric plan that describes development of your product in the pediatric population where it may be used. Please be aware that whether or not this pediatric plan and subsequent submission of pediatric data will be required depends upon passage of legislation or the success of the third party appeal. In any event, we hope you will decide to submit a pediatric plan and conduct the appropriate pediatric studies to provide important information on the safe and effective use of this drug in the relevant pediatric populations.

The pediatric exclusivity provisions of FDAMA as reauthorized by the Best Pharmaceuticals for Children Act are not affected by the court's ruling. Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products. You should refer to the Guidance for Industry on Qualifying for Pediatric Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request". FDA generally does not consider studies submitted to an NDA before issuance of a Written Request as responsive to the Written Request. Applicants should obtain a Written Request before submitting pediatric studies to an NDA.

Chemistry Issues

1. An 18-month expiry is granted for Xanax® XR Tablets in the proposed container/ closure system [60 mL bottles of 60 tablets for all strengths and foil/foil blisters for 0.5mg and 1 mg tablets].

2. We have not completed validation of the regulatory methods. However, we expect to continue to work with you to resolve any problems that may be identified.

Biopharmaceutics Issues

1. The following agreed upon dissolution method and specification has been approved for all strengths of Xanax® XR Extended-release Tablets:

Apparatus: USP apparatus I at 100 rpm
Medium: 500 ml of pH 6.0 buffer at 37°C
Specification: see Table below

	(b)-----	------	------	------
1 hour	----------	----------	----------	----------
4 hours	---------	---------	---------	---------
8 hours	---------	---------	---------	---------
16 hours	----------	----------	----------	----------

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division 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

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 should have any questions, please call Ms. Anna Marie H. Weikel, R.Ph., Senior Regulatory Project Manager, at (301) 594-5535.

Sincerely,

{See appended electronic signature page}

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Russell Katz
1/17/03 11:28:32 AM