DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville MD 20857

NDA 20-859

Wyeth-Ayerst Laboratories
Attention: Roy J. Baranello, Jr.
Senior Director, U.S. Regulatory Affairs
P. O. Box 8299
Philadelphia, PA 19101

Dear Mr. Baranello, Jr.:

Please refer to your new drug application (NDA) dated December 30, 1997, received January 6, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sonata[7] (zaleplon) 5 mg & 10 mg capsules.

We acknowledge receipt of your submissions dated:

February 17, 1999	February 26, 1999	April 9, 1999	April 12, 1999
May 10, 1999	June 4, 1999	June 7, 1999	July 8, 1999
July 12, 1999	July 13, 1999	July 22, 1999	July 29, 1999
August 10, 1999			

Your submission of February 26, 1999 constituted a complete response to our January 6, 1999 action letter.

This new drug application provides for the use of Sonata[7] (zaleplon) 5 mg & 10 mg capsules for the short-term treatment of insomnia.

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 labeling text. Accordingly, the application is approved effective on the date of this letter.

Labeling

The labeling accompanying this letter should be used for marketing this drug product. The attached final draft labeling is based on: 1) our labeling proposal sent to you via fax on July 6, 1999, 2) the changes agreed upon during the meeting held on August 4, 1999, and 3) your final labeling proposal submitted via fax on August 5, 1999. Additional changes were agreed upon and are documented in two August 10, 1999 faxes from your firm. These changes were pursuant to discussions regarding distribution of a patient package insert (PPI) in a teleconference held on August 9, 1999.

Patient Package Insert (PPI)

During our recent discussions on the requirement for a PPI, we indicated that the text for the PPI is to be identical to the text provided under the INFORMATION FOR PATIENTS TAKING

SONATA that is located at the end of the physicians= package insert. The PPI should be in a Afree standing@ form and available for distribution to the patient at the time the product is dispensed. This requirement is consistent with our requests for manufacturers of all benzodiazepine hypnotics and the non-benzodiazpine product zolpidem. This requirement was imposed due to concern about the misuse of hypnotics, particularly the use of these drugs for longer durations than is appropriate and their use in patients not adequately evaluated for the presence of underlying psychiatric or physical disorders that are manifested by insomnia.

Biopharmaceutics

1. Dissolution Specification

We agree, as proposed in your February 17, 1999 amendment, the dissolution specification for zaleplon should be set at NLT [ ] (Q = [ ]) at 20 minutes rather at NLT [ ] (Q = [ ]) in 10 minutes based on the current BCS classification of zaleplon, Class 1, i.e., highly soluble and highly permeable. Therefore, the dissolution method and specification for all capsule strengths of zaleplon should be as follows:

Apparatus:	USP Apparatus II
Medium:	900 mL water at 37 " 0.5^{1}C
Speed:	75 RPM
Specification:	Q = [ ] at 20 minutes

2. Drug-Drug Interactions

We remind you of your Phase 4 commitment specified in your submission dated February 26, 1999. This commitment, along with the completion date agreed upon, is restated below:

> You agreed to perform a drug interaction study with a stronger aldehyde oxidase inhibitor than cimetidine, i.e., promethazine, and indicated that the final study report for this study should be available by April 2000.

In addition, we recommend that you conduct, post-approval, *in vitro* assays with various prototypical CYP substrates in order to better understand the potential effects of zaleplon on the inhibition of other drugs.

Chemistry and Manufacturing Controls

We note that your July 8, 1999 amendment responds to our preliminary notice of chemistry and manufacturing controls issues that were conveyed to you in our June 30, 1999 letter. We also note that most of these issues were discussed during a teleconference held on July 23, 1999. In regard to deficiencies, we have the following comments and requests:

1. [ ].

2. [ ]

3. [ ]

4. Your proposed 36 month shelf life is acceptable based on the data submitted.

Pediatric Studies

As of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens must contain an assessment of the safety and effectiveness of the product in pediatric patients unless FDA waives or defers the requirement (63 F.R. 66632) (21 CFR 314.55 (or 601.27)). The Agency has not made a determination if a health benefit would be gained by studying zaleplon in pediatric patients for its approved indication. FDA is deferring submission of the pediatric assessments of safety and effectiveness that may be required under these regulations because pediatric studies should be delayed until additional safety or effectiveness data have been collected and reviewed. FDA will inform you on or before February 1, 2000 whether pediatric studies are required under the rule. If FDA determines at that time that pediatric studies are necessary, FDA will also set a specified time at which you must submit the required assessments.

Promotional Material

Submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Division of Drug Marketing, Advertising
and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package

insert and text for the patient package insert) and submitted labeling (immediate container and carton labels submitted on April 9, 1999 and July 12, 1999. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Submit twenty (20) copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Individually mount ten (10) of the copies on heavy-weight paper or similar material. For administrative purposes, the submission should be designated AFPL@ for approved NDA 20-859. Approval of this submission by FDA is not required before the labeling is used.

Submit one market package of the drug product 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, contact, Merril J. Mille, R.Ph., Senior Regulatory Management Officer at (301) 594-5528

Sincerely yours,

Robert Temple, M.D.
Director
Office of Drug Evaluation I
Center for Drug Evaluation and Research