CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 19-627/S-035

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 19-627/S-035

AstraZeneca LP
1800 Concord Pike
P.O. Box 15437
Wilmington, DE 19850-5437

MAY 19 2000

Attention: Lisa DeLuca, Ph.D.
Director, Regulatory Affairs

Dear Dr. DeLuca:

Please refer to your supplemental new drug application dated May 21, 1999, received May 21, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Diprivan® (propofol) 1% Injectable Emulsion.

We acknowledge receipt of your submission dated June 10, 1999.

This supplemental new drug application proposes the use of Diprivan® (propofol) 1% Injectable Emulsion in the pediatric population for general anesthesia

We have completed the review of this application and it is approvable. Before this application may be approved, however, it will be necessary for you to submit revised labeling that incorporates the changes in the enclosed draft labeling for the drug.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Under 21 CFR 314.50(d)(5)(vi)(*b*), we request that you update your NDA by submitting all safety information you now have regarding your new drug. Please provide updated information as listed below. The update should cover all studies and uses of the drug including: (1) those involving indications not being sought in the present submission, (2) other dosage forms, and (3) other dose levels, etc.

1. Retabulation of all safety data including results of trials that were still ongoing at the time of NDA submission. The tabulation can take the same form as in your initial

submission. Tables comparing adverse reactions at the time the NDA was submitted versus now will certainly facilitate review.

2. Retabulation of drop-outs with new drop-outs identified. Discuss, if appropriate.

3. Details of any significant changes or findings.

4. Summary of worldwide experience on the safety of this drug.

5. Case report forms for each patient who died during a clinical study or who did not complete a study because of an adverse event.

6. English translations of any approved foreign labeling not previously submitted.

7. Information suggesting a substantial difference in the rate of occurrence of common, but less serious, adverse events.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, call Laura Governale, Pharm.D., Regulatory Project Manager, at (301) 827-7410.

Sincerely,

/S/

Cynthia McCormick, M.D.
Director
Division of Anesthetic, Critical Care, and
Addiction Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research