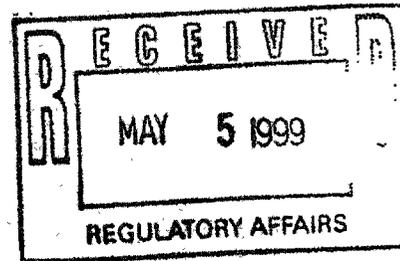




IND [REDACTED]



MAY 4

Shire Laboratories, Inc.

[REDACTED]
1550 East Gude Drive
Rockville, MD 20850

Dear [REDACTED]

Please refer to your Investigational New Drug Application (IND) dated March 25, 1999, submitted pursuant to section 505(l) of the Federal Food, Drug, and Cosmetic Act for SLI 381, a modified release Adderall® (Mixed Salts of a Single-Entity Amphetamine) product.

We also refer to your October 14, 1998, correspondence to IND [REDACTED], providing for an overview of your clinical development plan for the SLI 381 project, a longer acting version of Adderall, for the treatment of attention deficit hyperactivity disorder (ADHD) in children.

We have completed our review of your IND and we have no objection to the initiation of your proposed clinical study.

We would like to offer the following preliminary advice regarding your proposed clinical development plan:

1. Assuming that the time concentration profile for the modified release Adderall product will not be identical to that seen with bid dosing with immediate release Adderall, at least one adequate and well controlled clinical study in children with ADHD would be needed to support efficacy for this product. While the laboratory classroom type studies you are planning would provide useful preliminary information, it is preferred that you conduct at least one more traditional outpatient trial in a more typical clinic setting involving assessments in the child's usual environment by either parents or teachers. Ordinarily this would be a parallel group study of several weeks duration enrolling typical ADHD patients, including those with comorbid conditions, and having a primary outcome based on an assessment linked closely to the DSM-IV criteria for ADHD, e.g., the ADHD rating scale.
2. As we do not yet know the details of your plans for addressing the sprinkle route of administration, we are unable to provide any comment. We recommend that you consult with the Division further on this subject.

IND [REDACTED]

3. Since your proposed product will be part of the same class of amphetamine products, the class labeling rules for amphetamine products will also apply, with revisions as appropriate for a longer acting version.
4. We believe that a more detailed discussion of your clinical plans, including the pharmacokinetic program, for a longer acting ADDERALL^R product may be appropriate through a future meeting with the Division. Such a meeting may be arranged through the Division project manager.

You are responsible for compliance with the Federal Food, Drug, and Cosmetic Act and its implementing regulations promulgated there under. This includes reporting any unexpected fatal or life threatening experiences with the drug to FDA by telephone within three working days after receipt of the information (21 CFR 312.32), and the submission of annual progress reports at intervals not to exceed one year.

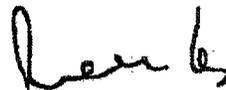
Your future submissions should be in triplicate and addressed as follows:

Division Director
Food and Drug Administration
Division of Neuropharmacological Drug Products (HFD-120)
Woodmont 2 Building
1451 Rockville Pike
Rockville, Maryland 20852

Each submission should be accompanied by a cover letter which identifies your IND number and the contents of your submission.

If you have any questions concerning this IND, please contact Ms. Anna M. Homonnay-Weikel, Project Manager, at (301) 594-5535.

Sincerely yours,



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