DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-961

AUG 26 1998

Isis Pharmaceuticals, Inc.
Attention: Mark W. Lotz, R.Ph.
Executive Director, Regulatory Affairs
2292 Faraday Avenue
Carlsbad, California 92008

Dear Mr. Lotz:

Please refer to your new drug application (NDA) dated April 6, 1998, received April 9, 1998, and submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vitravene Injection (fomivirsen sodium intravitreal injectable), 6.6 mg.

We acknowledge receipt of your submissions dated March 24, 30 and 31, April 23 and 30, May 8 (two) and 18, June 3, 23 and 29, July 1, 17, 29, 30 (two), and 31, and August 4, 7(two), 12, 14, 25 and 26, 1998.

This new drug application provides for the use of Vitravene Injection for the local treatment of cytomegalovirus (CMV) retinitis in patients with acquired immunodeficiency syndrome (AIDS) who are intolerant of or have a contraindication to other treatment(s) for CMV retinitis or who were insufficiently responsive to previous treatment(s) for CMV retinitis.

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

The final printed labeling (FPL) must be identical in content to the draft labeling submitted August 26, 1998. 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 30 copies of the FPL (package insert, immediate container and carton labels) as soon as it is available, in no case 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 20-961." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submissions. These commitments are listed below:

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

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 send one copy to the Anti-Inflammatory, Analgesic and Ophthalmic Drug Products and two copies of both the promotional materials 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

Please 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 Lori Gorski, Project Manager, at (301) 827-2090.

Sincerely,

Robert J DeLap 26 August 1998

Robert DeLap, M.D.
Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research