



NDA 21-087/S-002

Hoffmann-La Roche, Inc
Attention: Barbara S. Taylor, Ph.D.
Program Director, Drug Regulatory Affairs
340 Kingsland Street
Nutley, New Jersey 07110-1199

Dear Dr. Taylor:

Please refer to your supplemental new drug application dated May 22, 2000, received May 22, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tamiflu® (oseltamivir phosphate) Capsules 75mg.

We acknowledge receipt of your submissions dated:

July 21, 2000	October 11, 2000
July 25, 2000	October 18, 2000
August 8, 2000	October 19, 2000
August 10, 2000	October 20, 2000
August 18, 2000	November 6, 2000 (2)
August 22, 2000	November 10, 2000
August 31, 2000	November 14, 2000
September 1, 2000	November 16, 2000
September 28, 2000	

This supplemental new drug application provides for the use of Tamiflu (oseltamivir phosphate) 75 mg for the prophylaxis of influenza virus in adults and adolescents 13 years and older.

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.

The final printed labeling (FPL) must be identical to the enclosed draft labeling (package insert dated November 16, 2000, patient package insert dated November 16, 2000). 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 20 paper copies of the FPL 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. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 21-087/S-002." Approval of

this submission by FDA is not required before the labeling is used.

We remind you of your post marketing commitments specified in your submission dated November 16, 2000. These commitments, along with estimated completion dates, are listed below.

1. Please investigate the effectiveness and safety of oseltamivir for the treatment and prevention of influenza infection in immunocompromised patients. In this population the emergence of resistant viruses should be closely monitored. {Fourth quarter 2003}
2. Please study the pharmacokinetics and safety of oseltamivir, given at the proposed dosing regimens based on simulations, in end-stage renal dialysis subjects. {Fourth quarter 2003}
3. Please submit a final study report for the completed study of oseltamivir in subjects with impaired hepatic function. {Second quarter 2001}
4. Please submit a final study report for the completed long-term carcinogenicity studies in mice and rats. {July 31, 2002 (for mice) ; December 19, 2001 (for rats)}
5. Please explore the isolation, characterization and clinical implications of oseltamivir-dependent influenza virus variants. {To be discussed with the Agency second quarter 2001}

In addition, we remind you of the post marketing commitments for the treatment of influenza virus, previously agreed upon on October 25, 1999.

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. If an IND is not required to meet your post marketing commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(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 post marketing commitments must be clearly designated "Post Marketing Commitments."

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that at this time you have fulfilled the requirements of 21 CFR 314.55 for adolescents. We are deferring the requirement for studies in pediatric patients under 12 years of age for the indication of prophylaxis of influenza until December 31, 2004.

Please refer to the Written Request issued by this Division on March 1, 2000 for the study of Tamiflu in pediatric patients for the indication of treatment of influenza virus.

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

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Ms. Grace N. Carmouze, Regulatory Project Manager, at (301) 827-2335.

Sincerely,

Debra B. Birnkrant, M.D.
Acting Director
Division of Antiviral Drug Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research

Enclosure