DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021087/S-070
NDA 021246/S-053

SUPPLEMENT APPROVAL

Hoffmann-La Roche, Inc.
Attention: Peggy Omoruan
Program Manager, Regulatory Affairs
c/o Genentech, Inc.
1 DNA Way
South San Francisco, CA 94080

Dear Ms. Omoruan:

Please refer to your Supplemental New Drug Applications (sNDAs) dated and received on June 14, 2018, and your amendments, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for TAMIFLU® (oseltamivir phosphate) 30, 45, and 75 mg capsules, (NDA 021087) and TAMIFLU® (oseltamivir phosphate) powder for oral suspension, 6 mg/mL, (NDA 021246).

These Prior Approval supplemental new drug applications provide for updates to the US Prescribing Information as follows:

- **SECTION 8, "USE IN SPECIFIC POPULATIONS"**: Updated to comply with the Pregnancy and Lactation Labeling Rule (PLLR).
- **SECTION 12, "CLINICAL PHARMACOLOGY"**: A hemagglutinin (HA) substitution selected in cell culture and associated with reduced susceptibility to oseltamivir was revised to read KI73E, (previously read K173G).
- **SECTION 13, "NONCLINICAL TOXICOLOGY"**: The approximated human systemic exposure ($AUC_{0\text{-}24h}$) of oseltamivir carboxylate was revised based on the highest dose used in a fertility and early embryonic development study in rats.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

WAIVER OF ½ PAGE LENGTH REQUIREMENT FOR HIGHLIGHTS

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of Prescribing Information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the Prescribing Information, Patient Package Insert and Instructions for Use), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also, within 14 days, amend all pending supplemental applications that include labeling changes for these NDAs, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in Microsoft Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes. To facilitate review of your submission(s), provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients (which includes new salts and new fixed combinations), new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication in pediatric patients unless this requirement is waived, deferred, or inapplicable.

Because none of these criteria apply to your applications, you are exempt from this requirement.

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Suzanne Strayhorn, Regulatory Project Manager, at (240) 402-4247.

Sincerely,

{See appended electronic signature page}

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

ENCLOSURE(S):
Content of Labeling
Prescribing Information
Patient Package Insert
Instructions for Use