CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-257s000

21-304s007

OTHER ACTION LETTERS

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-257

COMPLETE RESPONSE

Hoffmann-La Roche Inc.
Attn: Snehal Shah, Pharm.D.
Program Manager, Pharma Development Regulatory
340 Kingsland Street
Nutley, NJ 07110-1199

Dear Dr. Shah:

Please refer to your new drug application (NDA) dated April 30, 2008, received May 1, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Valcyte® (valganciclovir hydrochloride) for oral solution. Please note that for administrative purposes, we have assigned a new NDA number [redacted] (b) (4) Our response to these [redacted] (b) (4) is addressed in a separate letter.

We acknowledge receipt of your amendments dated:

May 21, 2008	May 28, 20008	June 13, 2008
June 17, 2008	July 11, 2008	July 18, 2008
July 29, 2008	August 15, 2008	September 26, 2008
October 10, 2008	October 20, 2008	October 22, 2008
October 24, 2009	October 29, 2008	November 4, 2008
November 6, 2008		

This new drug application provides for the use of Valcyte® (valganciclovir hydrochloride) for oral solution for prevention of cytomegalovirus disease in pediatric kidney and heart transplant patients at high risk.

We have completed the review of your application, as amended, and have determined that we cannot approve this application in its present form. Before the application may be approved, you must address the following:

CLINICAL PHARMACOLOGY

Based on the findings from the analytical inspection at [redacted] (b) (4) [redacted] (b) (4) the plasma concentration data from WP16726 and CASG109 are not acceptable as submitted in the NDA. To assure the accuracy of analytical runs and the resulting drug concentrations, please provide the following information:

1. Provide frozen stability data that cover the duration of storage (b) (4) (b) (4) of all the plasma samples used for the quantification of ganciclovir in studies WV16726 and CASG109.
2. Identify a set of integration parameters and re-integrate all the chromatograms within a run in a consistent manner. This procedure should be repeated for all the chromatograms generated in studies WV16726 and CASG109. Use the resulting concentrations to repeat the pharmacokinetic and/or pharmacodynamic evaluations in studies WP16726 and CASG109.

LABELING

We reserve comment on the proposed labeling until the application is otherwise adequate. If you revise labeling, your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html.

Within one year after the date of this letter, you are required to resubmit or take one of the other actions available under 21 CFR 314.110. If you do not take one of these actions, we will consider your lack of response a request to withdraw the application under 21 CFR 314.65. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA Guidance for Industry *Formal Meetings With Sponsors and Applicants for PDUFA Products*, February, 2000 (http://www.fda.gov/cder/guidance/2125fnl.htm).

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call David Araojo, Pharm.D., Regulatory Project Manager, at (301) 796-0669.

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Debra Birnkrant
11/25/2008 04:39:49 PM
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