



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

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To: Debra B. Birnkrant, M.D., Division Director
Division of Anti-Viral Products (DAVP)
Office of Antimicrobial Products (OAP)

Thru: Ann McMahon, M.D., Deputy Director
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Subject: Analyses of Neuropsychiatric Events in Health Claims Database Studies
submitted on October 29, 2007

Drug Name(s): Tamiflu (Oseltamirvir phosphate)

Submission Number: IND 53,093 NDA21-087/S-33, NDA 21-246/S-021

Applicant/sponsor: Hoffman- La Roche Inc

OSE RCM #: 2007-828

The Division of Anti-Viral Products (DAVP) Office of Antimicrobial Products (OAP) requested the Office of Surveillance and Epidemiology, Division of Drug Risk Evaluation (DDRE/OSE) review for comment four health claims database studies sponsored by Roche that investigate the safety and effectiveness of Tamiflu (oseltamivir phosphate.) This submission was in response to the November 2005 Pediatric Advisory Committee meeting during which Roche offered to evaluate health care claims databases on health related and neuropsychiatric events in oseltamivir treated versus non-antiviral treated patients.

The sponsor submitted a report, March 16, 2007, on four studies and DDRE evaluated their submission. As a result, FDA requested through fax on September 6, 2007 via the sponsor that the investigators analyze their data differently. Specifically, FDA requested that outcomes to be stratified by appropriate age groups, provide more information on how neuropsychiatric outcomes were defined, and restrict their analysis to events that occurred within 14 days of receiving an influenza diagnosis. The submission dated October 25, was in response to this request and is currently under review.

In preparation for the Pediatric Advisory Committee meeting, the sponsor also submitted an additional analysis dated October 29 that specifically addresses the association between psychiatric events and oseltamivir using two health claims datasets that had previously been analyzed. We will not be able to evaluate completely their October reports in time to submit to the Pediatric Advisory committee for the November 27 meeting. The sponsors conclude, "There is no association seen between oseltamivir and neuropsychiatric events in the two matched cohorts." At the same time, it is important to keep in mind that given the difficulty to capture idiosyncratic psychiatric events, such as the ones recorded in AERS using MedDRA terms, it may not to be fully captured in health claims data.