DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FOI

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TRANSMITTED VIA FACSIMILE

Cynthia Dinella, Pharm.D.
Drug Regulatory Affairs
Hoffmann-La Roche
340 Kingsland Street
Nutley, New Jersey 07110-1199

Re: NDA 20-896
Xeloda (capecitabine) Tablets
MACMIS ID# 6738

Dear Dr. Dinella:

This letter is in reference to Hoffmann-La Roche's (Roche) May 5, 1998, submission of a proposed Dear Doctor letter with attached press release for Xeloda. In your letter, Roche notes that the press release had been disseminated the previous week. DDMAC has reviewed this press release and finds that it is misleading in violation of the Federal Food, Drug, and Cosmetic Act and applicable regulations for the following reasons:

The press release is misleading because it implies greater efficacy for Xeloda than has been demonstrated, given the basis for approval, that is, effects on surrogate markers. Some examples include the following:

(1) "We anticipate that Xeloda will help redefine chemotherapy."

(2) "At last, patients can take an effective pill, in their homes, to treat their cancer."

The second statement is also false and misleading because it implies that there are no other oral chemotherapy agents for the treatment of advanced breast cancer.

Further, the press release fails to include the full indication from the approved product labeling as discussed in our April 29, 1998, letter. It is important to include the full indication to communicate the nature of the accelerated approval; e.g., that approval is based on intermediate effects (response rate) and that no results are available from controlled trials confirming

clinical benefit such as improvement in disease-related symptoms, disease progression, or survival.

The press release is also misleading because it is not consistent with the approved product labeling. Examples include, but are not limited to, the following:

- "Xeloda caused minimal hair loss and limited bone marrow depression."

In fact, bone marrow suppression was a common side effect of Xeloda therapy (total incidence neutropenia (26%), thrombocytopenia (24%), and anemia (72%). Further, the presentation of this statement prior to the discussion of more serious risks minimizes the seriousness of the warnings and adverse events. In the clinical studies, 42% of patients receiving Xeloda experienced grade III or IV treatment-related adverse events.

DDMAC requests that Roche immediately discontinue the dissemination and use of the press release and any other promotional materials that contain similar themes. DDMAC requests that Roche submit a written response to this letter no later than June 22, 1997.

Please address any comments or questions that you may have to the undersigned at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm. 17B-20, 5600 Fishers Lane, Rockville, MD 20857 or by facsimile (301-594-6771). In all future correspondence related to this matter, please refer to MACMIS ID #6738.

Sincerely,

/S/

Anne M. Reb, MS, NP
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications