DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

JUL 19 1999

Ms. Peggy Jack
Program Director
Drug Regulatory Affairs
Hoffmann-La Roche Inc.
340 Kingsland Street
Nutley, NJ 07110-1199

Re: **NDA 20-766**
Xenical (orlistat tetrahydrolipstatin)
MACMIS ID # 8089

Dear Ms. Jack:

As part of its routine monitoring program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional material for Xenical (orlistat tetrahydrolipstatin) that is lacking in fair balance or otherwise misleading. Reference is made to the "Weight and See Computerized Reshaping Program" at the 81st Annual Endocrine Society Meeting held in San Diego on June 12-15, 1999 (Meeting). The dissemination of this material by Hoffmann-La Roche Inc. (H-R) violates the Federal Food, Drug, and Cosmetic Act (Act) and its implementing regulations. DDMAC requests that the use of the above referenced material and those containing the same or similar violations cease immediately.

Unsubstantiated Effectiveness Claims

Utilizing the computer re-shaping program to promote Xenical, H-R makes several claims of efficacy that are unsubstantiated. For example, a promotional labeling piece (printout) listing the results of the re-shaping program makes claims about the change in an individual's relative risk of coronary heart disease, type 2 diabetes, and hypertension relative to the change seen in that person's body mass index (BMI). This presentation implies that taking Xenical will decrease a person's BMI while decreasing their risk of other clinical conditions. These claims of effectiveness not only overstate the expected efficacy of Xenical (i.e., not all patients will lose weight and see a decrease in their BMI as a result of using Xenical), but they also imply effects of Xenical that have not been demonstrated by substantial evidence (i.e., reduction in risk of

coronary heart disease, type 2 diabetes, and hypertension). Thus, the computerized program and accompanying labeling pieces disseminated by H-R are misleading and in violation of the Act.

Minimizing the Risks Associated with Xenical Therapy

DDMAC is also concerned about the misleading promotion of Xenical by H-R Sales Representatives at the Meeting. On two separate occasions, two different H-R Sales Representatives minimized the side effects associated with Xenical therapy. For example, when asked by a clinician if there were any risks associated with Xenical therapy, the representative indicated that there was little-or-nothing to worry about because once a patient's body adjusts to the medicine usually within a couple of weeks and once they comply with the recommended diet, the side effects will disappear.

DDMAC is concerned that H-R's promotion of Xenical is misleading clinicians into believing that Xenical is a prescription drug without any side effects when quite the opposite is true. In fact, the approved product labeling (APL) for Xenical lists several side effects that occur with much greater frequency relative to placebo such as: oily spotting, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, increased defecation, and fecal incontinence. Additionally, although the frequency of reported side effects may have decreased during the second year of the study, there is no evidence to support that this was due to a patient's compliance to a "recommended" diet or that a patient's body will adjust to the medicine within two weeks as indicated by your representatives.

H-R should immediately cease using the computerized re-shaping program to the extent it makes unsubstantiated risk reduction claims, and all other promotional materials and activities for Xenical that contain the same or similar claims or presentations discussed in this letter. H-R should submit a written response to DDMAC, on or before August 1, 1999, describing its intent and plans to comply with the above. In its letter to DDMAC, H-R should include a list of all promotional materials and activities that were discontinued, and the discontinuation date.

H-R should direct its response to the undersigned by facsimile at (301) 594-6771, or by written communication at the Division of Drug Marketing, Advertising, and Communications, HFD-40; Room 17B-20; 5600 Fishers Lane; Rockville, MD 20857. DDMAC reminds H-R that only written communications are considered official.

In all future correspondence regarding this matter, please refer to MACMIS #8089 and NDA 20-766.

Sincerely,

Michael A. Misocky R.Ph., J.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications