DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

F.01

DEC 23 1998

TRANSMITTED VIA FACSIMILE

Michael P. Bigelow
Attorney
Eli Lilly and Company
Lilly Corporate Center
Indianapolis, IN 46285

Re: **NDA 20-815**
Evista (raloxifene hydrochloride)
MACMIS ID #7431

Dear Mr. Bigelow:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials for Evista (raloxifene hydrochloride) disseminated by Eli Lilly and Company (Lilly) that are in violation of the Federal Food, Drug, and Cosmetic Act (the Act) and applicable regulations. We specifically refer to a Lilly press release dated December 11, 1998. This press release promotes Evista for unapproved new uses and is lacking in fair balance. Our specific objections are outlined below.

Unapproved New Uses

In general, a sponsor shall not represent in a promotional context that a product is safe or effective for a use for which that product is under investigation or otherwise promote the drug. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including the dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug for a use for which it is under investigation and to preclude commercialization of the drug before it is approved for commercial distribution. DDMAC has reviewed the December 11th press release disseminated by Lilly, and has determined that it promotes Evista for a purpose not permitted in the approved product labeling (APL) and which, in fact, is in direct contradiction to the APL. The press release promotes Evista for the reduction in breast cancer risk among postmenopausal women. Whereas, the only indication for which Evista is currently approved is for the prevention of osteoporosis in postmenopausal women.

In the press release, Lilly states that "...Evista (raloxifene hydrochloride), Eli Lilly and Company's osteoporosis drug, reduces the incidence of newly-diagnosed invasive breast cancer, potentially the most serious type of breast cancer, by 63 percent among postmenopausal women taking the therapy for more than three years." Furthermore, the press release makes the broad promotional claims that "...Evista has a significant, positive impact on a woman's health after menopause" and that "This is a significant breakthrough in women's health". At the same time, Lilly states that the reduction in the risk of breast cancer is the direct result of new scientific findings from osteoporosis studies. However, Lilly makes virtually no attempt to disclose the specific findings that allegedly support these claims. While DDMAC might not object to an unbiased and scientific reporting of this newly available clinical data, Lilly has gone far beyond this with these broad, conclusive statements.

DDMAC notes the recent labeling change which describes the number of cases of newly-diagnosed invasive breast cancer in patients treated with either Evista or placebo in clinical trials. However, the following statement was also added, "The effectiveness of raloxifene in reducing the risk of breast cancer has not yet been established." Despite, and, in fact, in disregard to this statement, Lilly promoted Evista for this use in direct contradiction to the APL. The press release is therefore inconsistent with the APL and promotes Evista for an unapproved new use.

In a similar fashion, Lilly promotes Evista for the reduction in the risk of vertebral fracture. In the press release Lilly states that "Evista also has significant benefits on vertebral (spinal) fractures", "[S]pinal fractures reduced by half with three years of therapy", and "Taken together, Evista data validate the potential of SERMs to prevent osteoporosis and reduce the liklihood of fractures..." However, these claims directly contradict specific wording in the APL which state that, "The effects of EVISTA on fracture risk are not yet known."

Lacking in Fair Balance

Promotional materials are lacking in fair balance if they fail to present information relating to contraindications, warnings, precautions and side effects associated with the use of a drug in a manner reasonably comparable to the presentation of the information related to the effectiveness of the drug. The December 11th press release is lacking in fair balance. Set off by strongly worded headlines, Lilly presents close to three full pages of information related to safety and effectiveness claims for Evista. In contrast, Lilly provides one brief paragraph of risk information. Moreover, Lilly has failed to communicate an important contraindication to the use of Evista, i.e., that the use of Evista is contraindicated in women with active or a past history of venous thromboembolic events, including deep vein thrombosis, pulmonary embolism and retinal vein thrombosis.

Lilly should immediately discontinue the use of the press release and other promotional materials

that contain the same or similar representations for Evista discussed above. Lilly should submit a written response to DDMAC on or before January 4, 1998, listing the materials that will be discontinued and the date of discontinuation of these materials. Please address your response to the undersigned by facsimile at (301) 594-6771, or in writing at DDMAC, HFD-40, Room 17B-20, 5600 Fishers Lane, Rockville MD 20857.

In all correspondence related to this matter, please refer to MACMIS ID #7431 in addition to the NDA number. DDMAC reminds Lilly that only written communications are considered official.

Sincerely,

Jayne E. Peterson, R.Ph., J.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications