DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

TRANSMITTED VIA FACSIMILE

MAY 20 1998

Joseph S. Sonk, Ph.D.
Senior Director, Women's Healthcare Products
U.S. Drug Regulatory Affairs
Wyeth-Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-8299

RE: NDA #4-782
Premarin (conjugated estrogens) Tablets
MACMIS #6663

Dear Dr. Sonk:

Through routine monitoring and surveillance, the Division of Drug Marketing, Advertising and Communications has become aware of a direct-to-consumer (DTC) broadcast advertisement for Premarin (conjugated estrogens) Tablets that is false or misleading, and in violation of the Federal Food, Drug and Cosmetic Act. The advertisement, entitled "Everyday," was submitted to DDMAC by Wyeth-Ayerst (Wyeth) on Form FDA 2253 upon initial dissemination, as required by 21 CFR §314.81(b)(3)(i).

Reference is made to the May 19,1998, telephone conversation between Mr. Thomas Abrams, Dr. Nancy Ostrove, and Dr. Lisa Stockbridge, of DDMAC, and yourself, in which DDMAC requested that the advertisement be immediately withdrawn.

Specifically, DDMAC has the following objections to the advertisement:

1. The advertisement is lacking in fair balance or otherwise misleading because the communication of critical information relating to the risks of this product is inadequate. Specifically,

   - The boxed warning is minimized by the lack of an appropriately prominent presentation that would ensure that viewers are aware of this critical information. The boxed warning concerning the risk of uterine cancer is further minimized by the subsequent statement that "adding a progestin greatly reduces this risk." This latter statement is

also misleading because it implies that Premarin contains a progestin when, in fact, Premarin contains only estrogen.

- The boxed warning concerning use in pregnancy ("[p]regnant women should not take estrogen") is minimized because it omits the important contextual information that there is a possible risk to the fetus.

- The required statement of major side effects and contraindications omits side effects important to women, such as blood clots, nausea and vomiting and breast tenderness.

- In general, the risk information is not presented in a manner comparable to the presentation of efficacy information. For example, multiple distracting visual images and activity occur during the audio presentation of the risk information. In contrast, the efficacy information is presented against a static, non-distracting visual background.

2. The advertisement is misleading because it implies that Premarin can be used for a broader indication than that supported by substantial evidence. This is implied by statements like "everyday they're discovering more about estrogen loss," "...protect against future health problems," and "...can affect my health in a lot of ways." The approved product labeling (PI) for Premarin states that, in women, it is indicated for vasomotor symptoms associated with the menopause, atrophic vaginitis, the prevention and management of osteoporosis, certain forms of hypoestrogenism, and the palliative treatment of breast cancer. Moreover, Premarin's only prevention indication is for osteoporosis.

3. The advertisement is misleading because the generic name is not presented in a legible manner that is easily readable

DDMAC reminds Wyeth that comments in our accompanying letter, dated May 20, 1998, would also apply to this advertisement.

DDMAC requests that Wyeth immediately withdraw this DTC advertisement from use, as well as any other materials bearing the same or similar violative information. Further, DDMAC requests that Wyeth provide DDMAC, in writing, with its methods for removing these materials from the marketplace. Wyeth's response should be received no later than June 3, 1998.

If Wyeth has any questions or comments, please contact the undersigned by facsimile at (301) 594-6771, or at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, rm.17B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds you that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID #6663 in addition to the NDA number.

Sincerely,

Lisa L. Stockbridge, Ph.D.
Regulatory Review Officer
Division of Drug Marketing,
Advertising and Communications