DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

JUL 20 1998

TRANSMITTED VIA FACSIMILE

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#s** 17-612, 17-802, 18-668, 18-782, 19-190, 19-192, 20-683
Alesse (levonorgestrel and ethinyl estradiol) Tablets
Lo/Ovral (norgestrel and ethinyl estradiol) 21 & 28 Day Tablets
Nordette (levonorgestrel and ethinyl estradiol) 21 & 28 Day Tablets
Triphasil (levonorgestrel and ethinyl estradiol) 21 & 28 DayTablets
MACMIS ID# 6857

Dear Dr. Sonk:

Through routine monitoring and surveillance, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed various promotional materials for Alesse, Lo/Ovral, Nordette, and Triphasil Tablets, submitted by Wyeth-Ayerst Laboratories (Wyeth) on Form FDA 2253, that are considered to be false, misleading, or otherwise in violation of the Federal Food, Drug and Cosmetic Act. These materials include but are not limited to a journal ad (ID# 74929-00), brochures (ID# 64930-00, 64781-00, 64810-00, 64809-00), a cards (ID# LOV:262), sales aids (ID # 64982-00, FP-06), and posters (ID #64964-01, 22308-00).

Specifically, DDMAC has the following objections:

General

1. Claims that imply that one oral contraceptive is unique or superior to another oral contraceptive because of its dosing regimen are false or misleading because the different dosing regimens have not been demonstrated to have clinical significance in adequate and well-controlled comparative trials. Similarly, claims that imply that one oral contraceptive is unique or superior to another because of its progestin are false or misleading without substantiation from adequate and well-controlled clinical trials. For example, the depiction of Alesse,

Nordette, Triphasil, and Lo/Ovral as having specific characteristics that make them different from each other (i.e., Alesse is a "balanced combination that's just right for new starts," Triphasil is "trusted for excellent endometrial stability," Lo-Ovral is "the physician's first choice for more patients when it comes to switching OCs," and Nordette has "the patient acceptance of levonorgestrel") are misleading because there are no adequate and well-controlled studies that have demonstrated that any one of these is clinically significantly different from another or that any one of these is specifically indicated for a particular population or condition. Consequently, each of these oral contraceptives bears the same indication, efficacy, and safety information in its approved product labeling.

2. These materials are lacking in fair balance due to one or more of the following: (1) the claim "serious as well as minor adverse reactions have been reported following the use of all oral contraceptives..." is not adequate risk information (for example, the information in the black box warning is not included); (2) the bolded warning that oral contraceptives do not protect against sexually transmitted diseases is not included; and/or (3) the balancing information that is given is not presented with a prominence and readability that is reasonably comparable with the presentation of information relating to effectiveness.

   Nordette Promotional Materials

   The claim "the OC made specifically to meet the needs of your patients at risk for unintended pregnancy and STDs" is false or misleading because it implies that using Nordette helps prevent sexually transmitted diseases. According to the bolded warning on the approved product labeling for all oral contraceptives, "Patients should be advised that this product does not protect against HIV infection (AIDS) and other sexually transmitted diseases." DDMAC notes that this headline is associated with the "Safer Sex Initiative" for Nordette, however it is not clear from the headline, and the "Safer Sex Initiative" is associated only with a specific kit that includes a condom with the Nordette blister pack.

Triphasil Promotional Materials

1. The claim "no OC is better than Triphasil at reducing menstrual irregularities" is a false or misleading comparative claim that is not supported by data from adequate and well-controlled comparative clinical studies. A non-contraceptive health benefit of all oral contraceptives is reduction in menstrual irregularities.

2. The claim that Triphasil has "no surprises" is false and misleading because it implies that Triphasil has perfect efficacy and does not have the potential to cause adverse reactions. These "surprises" may occur with the product.

3. The claim that Triphasil offers "minimal metabolic impact" is false or misleading because it minimizes the risks for Triphasil. Further, the claim that Triphasil has a low incidence of androgenic side effects minimizes the fact that there are side effects, including those related to androgens, that may occur with the use of Triphasil.

4. The claims that Triphasil has the "world's #1 prescribed OC progestin" or that Triphasil is the "world's most prescribed triphasic OC formulation" are misleading without adequate substantiation, and the promotional materials for Triphasil lack adequate reference for these claims.

DDMAC requests that Wyeth immediately discontinue these and any other promotional materials, or activities, that involve the same or similar messages. Wyeth should respond, in writing, with its intent to comply with DDMAC's request by August 12, 1998. This response should include a list of all violative materials that will be discontinued and a description of Wyeth's plan for addressing the issue.

If you have 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 matter, please refer to the MACMIS ID # 6857 in addition to the NDA number.

Sincerely,

/S/

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