DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FDA

Food and Drug Administration
Rockville MD 20857

JUL 29 1998

TRANSMITTED VIA FACSIMILE

Doranne Frano
Associate Director, Regulatory Affairs
Searle
4901 Searle Parkway
Skokie, IL 60077

RE: **NDA#s** 18-160,18-168, 18-977
Demulen (ethynodiol diacetate and ethinyl estradiol) Tablets
Tri-Norinyl (norethindrone and ethinyl estradiol) Tablets
MACMIS ID# 6856

Dear Ms. Frano:

Through routine monitoring and surveillance, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has become aware of promotional materials for Demulen and Tri-Norinyl Tablets that are false, misleading, or otherwise in violation of the Federal Food, Drug and Cosmetic Act. These materials include but are not limited to journal ads (ID #A95WH111729T, A96DE11744T, A96DE12440T, A96WH13014T, C97TN13535T, C98TN14701T), brochures (#A96WH11850Q, A96DE12439Q, C97TN130560, C97TN13390Q, C97TN14200Q), visual aids (#A95DE11620Q, A96WH12176Q, A96WH12738Q, A96WH13024Q), file cards (#A96WH12998Q, A96WH12097Q, A96WH13023Q, A96WH12441Q-1,2,3, C97TN13464Q, C97TN13800Q), posters (#C97TN13185W, C97TN13771P, C97TN13227W), note pads (#C97TN13109P), notes (#C97TN13186A), and letters (A97TN13509A).

Specifically, DDMAC has the following objections:

General

1. Claims that imply that Tri-Norinyl is unique or superior to other oral contraceptives because of its dosing regimen are false or misleading because the different dosing regimen has not been demonstrated to have clinical significance in adequate and well-controlled comparative trials. For example, the campaign "Similar Yet Different" is false or misleading. The disclaimer regarding the lack of clinical significance, when it appears, is a small type font footnote that is not adequate to

dispel the misrepresentation that is emphasized in the materials for this campaign by headlines, bullets, and comparative charts depicting dosing regimens of other oral contraceptives as though there were a clinically significant difference among them.

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 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.

   Tri-Norinyl Promotional Materials

   Claims that imply that Tri-Norinyl is superior to other oral contraceptives because it does not cause weight gain (i.e., "an OC suited for the weight-conscious patient," "one way to measure her satisfaction with Tri-Norinyl") are false or misleading because they lack adequate substantiation from well-controlled clinical trials. This includes the graphics of a women's waistlines and association of Tri-Norinyl with BMI charts. It also includes charts that depict the mechanisms of progestin-mediated weight gain and surveys of physician or patient perception of weight gain.

   Demulen Promotional Materials

   Claims that imply that Demulen is superior to other oral contraceptives because of its low androgenic potential or low incidence of side effects (e.g., prevent acne, hirsutism, or oily skin) are false or misleading because they are not supported by adequate and well-controlled clinical trials.

DDMAC requests that Searle immediately discontinue these and any other promotional materials, or activities, that involve the same or similar messages. Searle 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 Searle'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 # 6856 in addition to the NDA number.

Sincerely,

/S/

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