DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

AUG - 6 1998

TRANSMITTED VIA FACSIMILE

Ron Lapré
Senior Director, Regulatory Affairs
Watson Laboratories, Inc.
311 Bonnie Circle
P.O. Box 1900
Corona, CA 91718-1900

RE: **NDAs 74-538, 72-721, 70-687, 73-594, 17-060**
Trivora (levonorgestrel and ethinyl estradiol, USP) Tablets
Zovia (ethnodiol diacetate and ethinyl estradiol, USP) Tablets
Necon (norethindrone and ethinyl estradiol) Tablets
Levora (levonorgestrel and ethinyl estradiol) Tablets
Nor-QD (norethindrone) Tablets
MACMIS # 6939

Dear Mr. Lapré:

Through routine monitoring and surveillance, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed various promotional materials for Trivora, Zovia, Necon, Levora, and Nor-QD Tablets, submitted by Watson Laboratories (Watson) 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 brochures (ID #s W-14003, W-10607a), a visual aid (ID # W-12018), and a hospital panel (ID # 12009).

Specifically, DDMAC has the following objections:

1. The materials are lacking in fair balance because the statement "serious as well as minor adverse reactions have been reported following the use of all oral contraceptives" is not adequate balance (for example, the boxed warning regarding cardiovascular risk and smoking and/or the bolded warning regarding the lack of protection against sexually transmitted diseases are not included). Similarly, "please see complete prescribing information...for contraindications, warnings, precautions, adverse reactions, and dosage and administration" is not adequate balance. Also, the risk information is

not presented with a prominence and readability that is reasonably comparable with the presentation of information relating to effectiveness.

2. Claims that imply that one oral contraceptive is unique or superior to another because of its dosing regimen or its progestin are false or misleading without substantiation from adequate and well-controlled clinical trials. For example, in brochure # W-10607a, the depiction of Trivora, Zovia, Necon, and Levora Tablets as having specific characteristics that make them different from each other (i.e., Zovia has "low androgenic potential, and Necon has "low risk of acne, oily skin, hirsutism, weight gain") is misleading because there are no adequate and well-controlled studies that have demonstrated that any one of these products is clinically significantly different from another or that any one of these products is specifically indicated for a particular population or condition. Similarly, there are no adequate and well-controlled studies that demonstrate that Trivora can "minimize androgenic side effects such as hirsutism, chronic anovulation, polycystic ovarian disease, acne, bloating and weight gain, reduced libido" (visual aid # W-12018). Furthermore, the statement that triphasic regimens "mirror the natural female cycle" is misleading because it implies, without adequate substantiation, that triphasic oral contraceptives are superior to other oral contraceptives because they have a quality that is more physiological (visual aid # W-12018). Consequently, each of these oral contraceptives bears the same indication, efficacy, and safety information in its approved product labeling.

The issues of overall fair balance and of androgenic side effects with Trivora have been previously discussed in correspondence with Watson. Thus, we are very concerned about these claims appearing in Watson's promotional materials.

DDMAC requests that Watson immediately discontinue these and any other promotional materials, or activities, that involve the same or similar messages. Watson should respond, in writing, with its intent to comply with DDMAC's request by August 20, 1998. This response should include a list of all violative materials that will be discontinued and a description of Watson'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 particular matter, please refer to MACMIS ID # 6939 in addition to the NDA number.

Sincerely,

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