DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

WARNING LETTER APR 7 2000

CERTIFIED MAIL - RESTRICTED DELIVERY
RETURN RECEIPT REQUESTED

Ref: 00-HFD-45-0201

Scott M. Dorfner, D.O.
Dorfner Family Medicine
1105 Sunset Road, Cooperstown Plaza
Burlington, New Jersey 08016

Dear Dr. Dorfner:

Between October 26 and November 23, 1999, Mr. Shirley Isbill, representing the Food and Drug Administration (FDA), met with you to: a) investigate allegations in an April 19, 1999, letter notifying FDA of your termination as a clinical investigator due to irregularities in signatures on study documentation, and b) review your conduct of the following clinical studies:

1. [ ] (Protocol No [ ] Study [ ] performed for [ ]
2. Clarithromycin (Protocol [ ] performed for Abbott,
3. Linezolid (Protocol [ ] performed for Pharmacia/Upjohn, and
4. Transdermal estradiol (Protocol [ ] and [ ] (Protocol [ ] performed for Berlex.

This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate clinical studies on which drug approval may be based and to assure that the rights and welfare of the human subjects of those studies have been protected.

From our evaluation of the inspection report, and the documents submitted with that report, we conclude that you did not adhere to pertinent federal regulations and/or good clinical investigational practices. We note that at the conclusion of the inspection, Mr. Isbill presented and discussed with you the items listed on Form FDA 483, Inspectional Observations. The inspectional observations include protocol violations and failure to maintain adequate and accurate records in the studies for which you are the principal investigator. We concur that in the conduct of your investigations you failed to meet your obligations as an investigator and remind you that you may delegate authority but responsibility remains with you. We wish to emphasize the following:

SUMMARY OF VIOLATIONS RELATED TO PERSONALLY CONDUCTING OR SUPERVISING THE CLINICAL INVESTIGATIONS (21 CFR 312.60)

You failed to personally supervise the clinical study which contributed to irregularities in your signature on study documents including FDA Form 1572, informed consents, and case report forms (CRFs) in which you admit that some of the signatures are in fact, not yours.

SUMMARY OF PROTOCOL VIOLATIONS (21 CFR 312.60)

You failed to conduct the following studies in accordance with the approved protocol.

1. Transdermal estradiol study (Protocol[ ]

   a. Subject 34001 was enrolled despite being amenorrheic for less than 6 months at screening (an exclusionary criterion).

   b. Subject 34002 was given a placebo patch to wear during screening; this placebo patch was part of the screening procedure for a different study (protocol[ ]

   c. Subject 34007 who had a history of suspected malignancy since 1991 (an exclusionary criterion) and unilateral oophorectomy, was enrolled without having FSH and estradiol levels measured at screening (an inclusionary requirement).

   d. Subject 34010's Pap smear at screening was "inadequate for evaluation", and was not repeated. Therefore, exclusionary Pap smear findings could not be evaluated.

   e. Subject 34804 was 39 years old at screening and signed a consent form although the minimum qualifying age for the study was 45 years.

2. [ ]study (Protocol[ ]

   a. Subjects 34001 and 34002 did not have a vaginal ultrasound (a required inclusionary test). Subject 34001 had a benign polyp (an exclusionary criterion) at the time of screening, and subject 34002 was found with a 20-mm endometrial thickening and a questionable blood-filled pocket. However, both were enrolled in the study.

   b. Subject 34004 did not have the required biopsy performed prior to inclusion in the study and no TSH test was done. However, this subject had a history of hypothyroidism, long-standing sleep apnea requiring a nasal C-PAP, and chronic depression (exclusionary criteria), yet was enrolled in the study.

3. [ ]study (Protocol[ ]

   Subject #0341001[ ]s medical records document "Tachypnea – absent," originally recorded on 12/8/98, was changed to "Tachypnea – mild" without explanation.

SUMMARY OF VIOLATIONS RELATED TO RECORDKEEPING AND CASE HISTORIES (21 CFR 312.62(b))

1. You failed to report all adverse events in the CRFs. In particular, subject #34010 (Protocol [ ]withdrew on 2/26/99 for skin irritation at the patch site, but this was not reported until July 1999, and subject 34004 (Protocol[ ]had sleep apnea and fluid retention, which was not reported

2. You failed to prepare and maintain adequate and accurate records in that CRFs for visits 2 and 3 for subject #0341002[ ]in the[ ]pneumonia study (Protocol[ ]were not completed although source documents show the subject returned for both visits.

Because of the departures from FDA regulations discussed above, we request that you inform this office, in writing, within 15 working days of your receipt of this letter, of the actions you have taken or plan to take to prevent similar violations in the future. Failure to adequately and promptly explain the violations noted above may result in further regulatory action.

If you have any questions, please contact Dr. Antoine El-Hage, at (301)594-1032, FAX (301)827-5290. Your written response and any pertinent documentation should be addressed to:

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Branch Chief
Good Clinical Practice II, HFD-47
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place
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Sincerely,

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