



Food and Drug Administration
Rockville MD 20857

SEP 13 2000

NOTICE OF INITIATION OF DISQUALIFICATION PROCEEDINGS AND OPPORTUNITY
TO EXPLAIN LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Roger D. Anderson, M.D.
Anderson Clinical Research, Inc.
3339 Ward Street
Pittsburgh, Pennsylvania 15213-4330

Dear Dr. Anderson:

Between April 12 and August 4, 1999, Ms. Cynthia L. Rakestraw and Ms. Gladys B. Casper, representing the Food and Drug Administration (FDA), met with you to review your conduct of a clinical study (protocol [] of the investigational drug [] capsules [] performed for []

This inspection is part of the 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 are protected.

Based on our evaluation of information obtained, the Center for Drug Evaluation and Research of FDA (Center) believes that you have repeatedly or deliberately violated regulations governing the proper conduct of clinical studies involving investigational new drugs as published under Title 21, Code of Federal Regulations (CFR), Part 312 (copy enclosed) and that you submitted false information to FDA or the sponsor.

We reviewed your September 14, 1999, response to the inspectional findings (Form FDA 483 dated August 4, 1999). While we accept your responses to items 2, 4, 7, 8, 9 and 10, we do not accept your responses to items 1, 3, 5 and 6, as detailed below.

This letter provides you with written notice of the matters under complaint and initiates an administrative proceeding, described below, to determine whether you should be disqualified from receiving investigational products as set forth under 21 CFR 312.70.

A listing of the violations follows. The applicable provisions of the CFR are cited for each violation.

In summary:

- I. You failed to personally conduct or supervise the clinical study, as you committed to do when you signed the Form FDA 1572 [21 CFR 312.53(c)(1)(vi)(c)], in violation of 21 CFR 312.60. Your lack of supervision caused the submission of false information to the sponsor in required reports for the study of investigational new drugs that are subject to section 505 of the Federal Food, Drug, and Cosmetic Act, as demonstrated by the violative conduct described more fully below.

- II. You submitted false information to the sponsor [21 CFR 312.70(a)].
 - A. Data derived from falsified electrocardiograms (ECGs) were submitted.
 1. The ECG for subject #002 [] on 10/3/97 is the same as the ECG for subject #001 [] on 10/31/97.
 2. The ECG for subject #007 [] on 11/19/97 is the same as the ECG for subject #008 [] on 11/21/97.
 3. The ECGs for subject #015 [] and #013 [] both done on 12/8/97, are the same.
 4. The ECG for subject #014 [] on 1/14/98 is the same as the ECG for subject #016 [] on 1/12/98.
 - B. The Physical Examinations (PEs) that you claim to have performed for at least 9 of 17 subjects are falsified. Six subjects [#007 [] #008 [] #009 [] #013 [] #014 [] and #015 []] have provided signed affidavits, two subjects [#016 [] and #017 []] have confirmed by telephone, and subject #010 [] has confirmed in person that you did not perform their PEs.

- III. You failed to maintain adequate and accurate records of all observations and other data pertinent to the investigation on each individual administered the investigational drug or employed as a control in the investigation, in violation of 21 CFR Parts 312.62(b). For example:
 - A. The original screening ECG strip (raw data) for subject #001 [] was not available for FDA inspection.
 - B. There was no contemporaneous documentation explaining the following changes on ECGs:
 1. The printed identification number (ID#) on the ECG ascribed to subject #001 [] on 10/31/97 is identified as #002 []

2. The date, time, ID#, sex, and age, on the ECG ascribed to subject #007 was handwritten after obliterating the printed information.
3. The ID# on the ECG ascribed to subject #011 [] was handwritten after obliterating the printed ID#.
4. The printed ID# on the ECG ascribed to subject #010 [] is identified as #009 []
5. The time and ID# on the ECG ascribed to subject #015 [] was overwritten by obliterating the printed information.
6. The printed ID# on the ECG ascribed to subject #003 [] is identified as #002 []
7. The ID# on the ECG ascribed to subject #008 [] on 11/21/97 was overwritten by obliterating the printed ID#.

Your response does not provide specific explanations for the above mentioned discrepancies, but in general you attribute them to an inadequate ECG machine utilized during the trial. However, you have not provided any documentation to identify the equipment used or any problems experienced with it during the study.

- C. For subjects #004 [] #005 [] #010 [], and #011 [] you inaccurately report on page 2 of the case report form (CRF) that each was using a stable dose of oral [] for a minimum of 7 days prior to his/her respective screening visit date.
- D. You did not report on page 9 of the CRF the reason for not performing the Visit 1 urinalysis for subjects #001 [] #002 [] and #006 []
- E. Throughout the CRF for subject #009 [] you inaccurately report the subject's initials as [] In addition, on page 7 of the CRF you report this subject's height is 52 inches, and confirmed this height on two data query forms dated 4/23/98 and 6/22/98, respectively. The FDA investigator who met and interviewed subject #009 [] reports that the subject was about 61 inches tall.

- IV. You failed to inform subjects when obtaining their informed consent of the potential risk of developing [] dependence and [] withdrawal effects as a result of their study participation, in violation of 21 CFR 50.25(a)(2) and 312.60. We note your response that "This consent form was supplied by the sponsor and used at multiple sites for this trial and was approved by my IRB." You also state that, "All subjects were required to be dosing with a minimum of [] prior to study entry." Your response to this deviation is

not acceptable because, our inspection and your response reveal that for seven out of seventeen subjects you extended their run-in phase to two weeks in order to stabilize them on [] and thereby meet eligibility status. You also acknowledge that the IRB was not notified of this deviation from protocol requirement. Furthermore, your argument that the risk of [] dependence or withdrawal was not included in the consent form because patients were already aware of this risk is not acceptable in light of the fact that the consent form does include other obvious discomforts of the needle insertion during blood draw, as well as eleven other common side effects of [] such as sleepiness.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical studies of investigational drugs. It is your responsibility to ensure adherence to each requirement of the law and relevant regulations.

On the basis of the above listed violations, the Center asserts that you have repeatedly or deliberately failed to comply with the cited regulations and repeatedly or deliberately submitted false information. The Center proposes that you be disqualified as a clinical investigator. You may reply in writing or at an informal conference in my office to the above stated issues, including an explanation of why you should remain eligible to receive investigational products and not be disqualified as a clinical investigator. This procedure is provided for by regulation 21 CFR 312.70.

Within fifteen (15) days of receipt of this letter, write or call me at (301)594-0020 to arrange a conference time or to indicate your intent to respond in writing. Your written response must be forwarded within thirty (30) days of receipt of this letter. Your reply should be sent to:

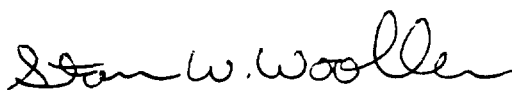
Stan W. Woollen
Acting Director
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place, Room #103
Rockville, Maryland 20855

Should you request an informal conference, we ask that you provide us with a full and complete explanation of the above listed violations. You should bring all pertinent documents with you, and a representative of your choosing may accompany you. Although the conference is informal, a transcript of the conference will be prepared. If you choose to proceed in this manner, we plan to hold such a conference within 30 days of your request.

At any time during this administrative process, you may enter into a consent agreement with the Center regarding your future use of investigational products. Such an agreement would terminate this disqualification proceeding. Enclosed you will find a proposed agreement between you and the Center.

The Center will carefully consider any oral or written response. If your explanation is accepted by the Center, the disqualification process will be terminated. If your written or oral responses to our allegations are unsatisfactory, or we cannot come to terms on a consent agreement, or you do not respond to this notice, you will be offered a regulatory hearing before FDA, pursuant to 21 CFR 16 (enclosed) and 21 CFR 312.70. Before such a hearing, FDA will provide you notice of the matters to be considered, including a comprehensive statement of the basis for the decision or action taken or proposed, and a general summary of the information that will be presented by FDA in support of the decision or action. A presiding officer free from bias or prejudice and who has not participated in this matter will conduct the hearing. Such a hearing will determine whether or not you will remain entitled to receive investigational products. You should be aware that neither entry into a consent agreement nor pursuit of a hearing precludes the possibility of a corollary judicial proceeding or administrative remedy concerning these violations.

Sincerely yours,



Stan W. Woollen
Acting Director
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research

Enclosures:

- #1 - 21 CFR 312
- #2 - 21 CFR 16
- #3 - Agreement