



WARNING LETTER

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Return Receipt Requested

MAY 25 1999

Jeffrey M. Adelglass, M.D.
Research Across America
9 Medical Parkway, Suite #202
Dallas, Texas 75234

Dear Dr. Adelglass:

Between November 16 and December 4, 1998, Mr. Phillip D. Waldron, from the Food and Drug Administration (FDA), inspected your conduct of a clinical study (Protocol Number [] of [] sponsored your study.

We reviewed (a) the inspection report; (b) the documents collected during the inspection; (c) the Inspectional Observations (i.e., Form FDA 483) provided to you at the conclusion of the inspection; (d) your January 29, 1998, letter to Ms. Carrier that informed us of the internal audit findings, which included invalid study data reporting; and (e) your December 10, 1998, written response to the Inspectional Observations. From our review of the documents listed above, we find that you failed to comply with the Federal regulations governing the study of investigational new drugs and the protection of human research subjects. Your violations are summarized below.

1. You failed to personally conduct or supervise your clinical study [21 CFR 312.53(c)(1)(vi)(c) and 312.60].

The problems listed below indicate that you, as the investigator, failed to ensure the study was conducted according to the signed investigator statement and the applicable Federal regulations.

2. You failed to prepare and maintain adequate and accurate records of all observations and other data pertinent to your study for each subject as required by Federal regulations [21 CFR 312.62(b) and 312.62(c)].

- a. For subject #001, the following records were not available during the inspection:
 - i. total testosterone laboratory report for the screening visit
 - ii. chemistry, hematology, and urinalysis laboratory reports for the screening and final visits
 - b. For subject #013, the following records were not available:
 - i. chemistry, hematology, and urinalysis laboratory reports for the final visit
 - ii. the subject's and partner's diaries
 - c. For subject #022, the patient chart did not have a record of the physical examination for the final visit
 - d. For subjects #014 and #015, the only records available were the chemistry, hematology, urinalysis, and total testosterone laboratory reports for the screening visit.
3. You failed to maintain adequate drug disposition records that included the dates, quantity, and use by subjects of the study drugs [21 CFR 312.62(a) and 312.62(c)].
- a. Records of the drug packet distribution were not available during the inspection for the following study numbers:

#012	packets 5-8
#014	packets 1-20
#015	packets 1-20
#016	packets 5-8
 - b. Packets 1-4 for subject #024 were missing and not accounted for. Your study had no subject assigned #024.
4. You failed to conduct your study in accordance with the approved protocol [21 CFR 312.53(c)(1)(vi)(a) and 312.60].
- a. You failed to list all concomitant medications on the case report forms for each subject as required by the protocol (section 5.2.1c).

- i. for subject #013, you failed to report Lasix and glipizide
 - ii. for subject #021, you failed to report prednisolone and testosterone
 - iii. for subject #022, you failed to report Zestoretic and Plendil
 - b. You failed to perform the screening tests (chemistry, hematology, and urinalysis) for subjects #006 and #009 until visit 3.
 - c. You failed to determine the total testosterone level for each subject at the screening visit as required by the protocol (protocol section 5.1).
 - i. for subject #002, the testosterone level was not determined until the final visit
 - ii. for subject #003, the testosterone level was not determined until two days after visit 5
 - iii. for subject #006, the testosterone level was not determined until visit 3
 - iv. for subject #009, the testosterone level was not determined until visit 3
 - d. You failed to exclude subjects with a testosterone level of less than [] ng/dl as required by the protocol (protocol section 4.2)
 - i. You enrolled subject #005 on September 18, 1997, without knowing his total testosterone level. The level was reported on September 19, 1997, as 269 ng/dl
 - ii. You enrolled subject #009 on September 22, 1997, without determining his total testosterone level. You did not obtain a specimen for determining that level until October 6, 1997 (visit 3). On October 8, 1997, the total testosterone level was reported as only 260 ng/dl.
5. You failed to obtain informed consent prior to a subject's participation in the study [21 CFR 50.20 and 312.62(b)].

The partner of subject #002 began her participation in your study on September 17, 1997, but she did not sign a consent form until October 1, 1997.

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The above description of our findings is not intended to be an all inclusive list of your violations and deficiencies.

We accept your explanation and assurance in your letters of January 29, 1998 and December 10, 1998, in which you stated that "measures have been instigated to prevent recurrence of the problem," and you listed these measures (e.g., increasing quality assurance (QA) activities, tracking subjects, reviewing prospective employees, and tracking employee time usage).

Because of the departures from FDA regulations discussed above, we request, within 15 working days of your receipt of this letter, that you provide this office a copy of your revised standard operating procedures (SOPs). Your SOPs must include all the procedures you have instituted to prevent a recurrence of problems similar to those noted above and must specify your involvement as the person conducting and/or supervising the studies. Your failure to provide us a copy of your SOPs that will ensure compliance with Federal regulations may result in regulatory action without further notice.

Your written response, including a current copy of your SOPs must be addressed to:

Bette L. Barton, Ph.D., M.D.
Division of Scientific Investigations (HFD-344)
Food and Drug Administration
7520 Standish Place, Suite 25
Rockville, Maryland 20855

Sincerely yours,



David A. Lepay, M.D., Ph.D.
Director
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research