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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

MAR 1 1 2008

Certified Mail
Return Receipt Requested

Reference No. 08-HFD-45-1101

Darren McDaniel
Chief Executive Officer
Coast Institutional Review Board
5475 Mark Dabling Blvd., Suite 351
Colorado Springs, CO 80918

Dear Mr. McDaniel:

Between July 10 and 18, 2007, Mr. James Fleckenstein, representing the Food and Drug Administration (FDA), inspected Coast IRB. The purpose of this inspection was to determine whether Coast IRB was in compliance with the regulations governing IRBs and those governing the protection of human subjects participating in clinical trials contained in Title 21 of the Code of Federal Regulations (CFR), Parts 56 and 50. These regulations apply to clinical investigations of products regulated by FDA. We are aware that at the conclusion of this inspection, our investigator presented and discussed with you a Form FDA 483, Inspectional Observations.

From our evaluation of the Form FDA 483, the establishment inspection report, the documents submitted with that report, and your written responses dated August 15 and November 29, 2007, we conclude that the IRB failed to adhere to certain requirements in 21 CFR Part 56 as described below. The regulatory violations were identified from the review of the IRB's written procedures and the review of the following study:

[ ]Protocol[ ] entitled "A Phase 1 Multi-Center, Open-Label, Randomized, 3-Arm Clinical Trial to Evaluate[ ]in the Treatment of[ ]

We wish to emphasize the following:

1. **The IRB failed to follow FDA regulations regarding expedited review procedures [21 CFR 56.110(b)].**

   The regulations require that under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the IRB chairperson from among the members of the IRB, and the IRB may use the expedited review process to review either or both of the following: (1) some or all of the research appearing on the Federal Register list and found by the reviewer(s) to involve no more than minimal risk, or (2) minor changes in previously approved research during the period for which approval is authorized. Coast IRB's written procedures for expedited review also reflect this requirement. As explained below, Coast IRB had an inexperienced member conduct the expedited review and reviewed research under expedited review that did not meet the criteria above.

   On March 19, 2007, you appointed Mr.[ ]to the IRB Board and instructed him to conduct an expedited review of the advertisement for the above referenced study. Mr. [ ]lacked the requisite relevant experience to conduct expedited review on behalf of the IRB. In addition, the advertisement reviewed under the expedited review procedure on March 19, 2007, did not qualify for expedited review under 21 CFR 56.110(b), as it was neither research appearing on the Federal Register list and found by the reviewer to involve no more than minimal risk nor minor changes to previously approved research. Finally, the advertisement was not appropriate for expedited review because the full IRB had met and reviewed it as discussed below.

   The full IRB considered the recruitment advertisement for the study at three previously convened meetings on March 1, 8, and 15, 2007. On March 1, 2007, the IRB approved the advertisement with changes and that decision was communicated to the sponsor. Upon resubmission by the sponsor, the IRB disapproved the recruitment advertisement for the above study on both March 8 and 15, 2007. The initial approval with changes and the subsequent disapprovals were based on the IRB's determination that the advertisement was coercive in nature. In each case, the IRB or the IRB Chair proposed alternative language which would have been acceptable to the Board.

   Despite the advertisement having been first approved with changes and then disapproved by the IRB, you appointed Mr.[ ]to the IRB Board on March 19, 2007, and then you directed Mr.[ ]to conduct an expedited review of the advertisement on that same day. On March 19, 2007, Mr.[ ]via expedited review, approved the advertisement in its original form which had previously been approved with changes and then disapproved as submitted by the full IRB. Despite the full board's consideration of this matter at three previous meetings, documentation of the disapprovals in the minutes of both March 8th and 15th, and e-mails that indicate otherwise, you stated that you were unaware of the Board's decisions on this matter.

   Furthermore, the regulations at 21 CFR 56.110(b) require that the IRB chairperson conduct expedited review or designate an experienced reviewer to conduct an expedited review on behalf of the IRB. You, in your capacity as the chief executive officer of the IRB, lacked the authority to designate anyone to conduct expedited reviews on behalf of the IRB.

Your written response of August 15, 2007, acknowledges that expedited review may only be conducted by the IRB Chair or by one or more experienced reviewers designated by the Chair from among the IRB members. This written response also states that all advertisement/recruitment materials that underwent expedited review by Mr.[ ]are being reviewed by the Chair for regulatory compliance. Neither this written response nor your written response of November 29, 2007, addresses the issue that you directed review of the research under expedited review when it did not qualify under FDA regulations for expedited review and that you had Mr.[ ]conduct an expedited review despite Mr. [ ]lack of relevant experience.

2. **The IRB did not follow written procedures for conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and institution [21 CFR 56.108(a)(1) and 56.110(c)].**

   As noted, the advertisement for the above referenced study was approved under an expedited review procedure. FDA's regulations require IRBs using an expedited review procedure to adopt a method for keeping all members advised of research proposals which have been approved under the procedure. Coast IRB's Standard Operating Procedure (SOP) Manual, Version 4, Section 4.1.1, stated that all regular members of the IRB were to be informed of such actions via the Coast IRB agenda. However, IRB members interviewed by FDA could not recall being notified about the expedited review and we were not able to locate an agenda with this expedited review listed as an agenda item. If Coast IRB has documentation notifying the IRB members about this expedited review, please provide it.

3. **The IRB did not maintain minutes of meetings in sufficient detail to indicate the actions taken by the IRB [21 CFR 56.115(a)(2)].**

   The minutes for the March 1, 2007, meeting do not document the IRB's approval with changes of the advertisement for the above study. Such information is required to be included in the minutes under the regulations. However, verbal statements from the IRB Chair during the inspection and a copy of the advertisement revised by the IRB Chair indicate that the advertisement was not approved as submitted.

We acknowledge your statements that you revised your standard operating procedures regarding minutes to include the meeting minute elements required by 21 CFR 56.115(a)(2), and that you hired an individual to specifically take IRB minutes.

This letter is not intended to be an all-inclusive list of deficiencies for the above referenced study reviewed by the full IRB and through expedited review. It is your responsibility to assure that Coast IRB's practices and procedures fully comply with all applicable statutes and regulations.

Under 21 CFR 56.110(d), FDA, in order to protect the rights or welfare of subjects, is suspending Coast IRB's use of expedited review procedures until further notice because of Coast IRB's failure to follow FDA regulations regarding the use of expedited review procedures. FDA will remove this suspension after receipt of a satisfactory response that addresses the IRB's inappropriate use of expedited review and that provides details concerning the corrective action taken.

Because of the departures from FDA regulations discussed above, please inform this office, in writing, within fifteen (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 without further notice.

If you have any questions, please contact Dr. Constance Lewin at [redacted] Your written response and any pertinent documentation should be addressed to:

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Good Clinical Practice Branch 1, Bldg. 51, Room 5354
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Sincerely yours,

Leslie K. Ball, M.D.
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cc:
[redacted] M.Ed.
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