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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Ref: 09-HFD-45-02-02

Eli Friedman, M.D.
Chairman, SUNY Downstate Medical Center IRB
Health Science Center
450 Clarkson Ave.
Brooklyn, NY 11203-2056

Dear Dr. Friedman:

Between September 22 and October 1, 2008, Ms. Alia Legaux, representing the Food and Drug Administration (FDA), inspected the Institutional Review Board (IRB) at the SUNY Downstate Medical Center/Health Science Center. The purpose of this inspection was to determine whether the IRB procedures for the protection of human subjects complied with Title 21 of the Code of Federal Regulations (CFR), Parts 50 and 56. These regulations apply to clinical studies of products regulated by FDA. We are aware that at the conclusion of the inspection our investigator presented and discussed with you, a Form FDA 483, Inspectional Observations.

From our review of the establishment inspection report and the documents submitted with that report, we conclude that the IRB did not adhere to the applicable statutory requirements and FDA regulations governing the protection of human subjects. We wish to emphasize the following:

1. The IRB failed to prepare the minutes of IRB meetings in sufficient detail to show actions taken by the IRB, the vote on actions, including the number of members voting for, against and abstaining [21 CFR 56.115(a)(2)].

   Our inspection revealed seven instances in which IRB E met and conducted significant IRB activity; however, no meeting minutes could be found. The following

table lists the dates of the meetings and a brief summary of the documentation to support our finding.

Date	Documentation
12/22/05	Sign-in sheet demonstrating quorum and IRB letter dated 12/23/05 for study (b) (4) which states "Your communication referenced above was reviewed at the 12/22/2005 meeting of the HSCB/KCHC Institutional Review Board."
9/12/06	Sign-in sheet demonstrating quorum and agenda for the meeting.
2/8/07	Sign-in sheet demonstrating quorum.
2/28/07	Sign-in sheet demonstrating quorum. The IRB letter dated 3/1/07 for study (b) (4) which states "The Board has received your application to close the study listed above. It was reviewed at the 2/28/2007 meeting of the HSCB/KCHC Institutional Review Board." The IRB letter dated 3/7/07 for study (b) (4) which states "This is to confirm that the adverse event dated 1/17/07 (Subject (b) (6)) related to the study listed above was reviewed at the 2/28/2007 meeting of the HSCB/KCHC Institutional Review Board."
7/5/07	Sign-in sheet demonstrating quorum, agenda for the meeting and IRB letter dated 7/17/07 for study (b) (4) which states "Your request for approval of the new study listed above was reviewed at the 7/5/2007 meeting of the HSCB/KCHC Institutional Review Board."
9/18/07	Sign-in sheet demonstrating quorum. Agenda for the meeting. IRB letter dated 9/19/07 for study (b) (4) which states "This is to confirm that the above adverse event(s) dated July 30, 2007 (Subject (b) (6)) related to study listed above was reviewed at the 9/18/2007 meeting of the HSCB/KCHC Institutional Review Board." IRB letter dated 9/26/07 for study (b) (4) which states "Your request for approval of the new study listed above was reviewed at the 9/18/2007 meeting of the HSCB/KCHC Institutional Review Board." IRB letter dated 9/27/07 for study (b) (4) which states "Your request for continuing review of the study listed above was reviewed at the 9/18/2007 meeting of the HSCB/KCHC Institutional Review Board." IRB letter dated 10/11/07 for study (b) (4) which states "Your request for approval of the new study listed above was reviewed at the 9/18/2007 meeting of the HSCB/KCHC Institutional Review Board." IRB letter dated 10/11/07 for study (b) (4) which states "Your request for approval of the new study listed above was reviewed at the 9/18/2007 meeting of the HSCB/KCHC Institutional Review Board."
11/8/07	Sign-in sheet demonstrating quorum and IRB letters dated 11/8/07 for study (b) (4) which states "Your request to reopen the study listed above was reviewed at the 11/8/2007 meeting of the HSCB/KCHC Institutional Review Board (Committee E)."

2. For other than expedited reviews, the IRB failed to review proposed research at convened meetings at which a majority of the members of the IRB are present,

including at least one member whose primary concerns are in non-scientific areas [21 CFR 56.108(c)].

Our inspection revealed an instance in which the IRB reviewed and approved research at meetings in which a quorum was not present. The meeting minutes for the February 14, 2007 meeting of IRB A state the "committee did not achieve quorum at this meeting so the meeting was adjourned". Despite this statement, there is strong evidence that IRB action occurred on this date as evidenced by the following IRB letters: the March 2, 2007 letters for study (b) (4) and study (b) (4) which states "Your response was reviewed at the 2/14/2007 meeting of the HSCB/KCHC Institutional Review Board."; the March 6, 2007 letter for study (b) (4) which states "Your request for continuing review of the study listed above was reviewed at the 2/14/2007 meeting of the HSCB/KCHC Institutional Review Board.", and finally, the March 6, 2007 letter for study (b) (4) and the March 8, 2007 letter for study (b) (4) which state "Your request for approval of the new study listed above was reviewed at the 2/14/2007 meeting of the HSCB/KCHC Institutional Review Board."

3. The IRB failed to follow its written procedures for conducting its continuing review of research and for reporting its findings and actions to the investigator and the institution [21 CFR 56.108(a)(1)].

   Our inspections revealed several instances in which the IRB failed to follow its written procedures for conducting continuing review of ongoing research.

   For Protocols (b) (4) there is no documentation in the IRB files that the investigators were ever provided renewal reminder notices alerting them to upcoming continuing review dates as required in the IRB written procedures under the section entitled "Annual Progress Reports and Continuing Review Requirements" which states "Renewal reminder notices will be mailed to investigators by the IRB Office two months prior to expiration of approval".

This letter is not intended to be an all-inclusive list of deficiencies for the protocols reviewed and approved by the IRB. It is your responsibility to ensure that SUNY Down State Medical Center/Health Service Center IRB's practices and procedures fully comply with all applicable statutes and regulations. Because of the departures from FDA regulations discussed above, either the IRB or its parent institution should 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 regulatory action without further notice.

If you have any questions, please contact Constance Lewin, M.D., M.P.H., at 301-796-3397; FAX 301-847-8748. Your written response and any pertinent documentation should be addressed to:

Constance Lewin, M.D., M.P.H.
Branch Chief, Good Clinical Practice Branch I

Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Bldg 51, Room 5354
10903 New Hampshire Avenue
Silver Spring, MD 20993

Sincerely yours,

{See appended electronic signature page}

Leslie K. Ball, M.D.
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research

cc: (b) (6), M.D.
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/s/

LESLIE K BALL
02/11/2009