Inspections, Compliance, Enforcement, and Criminal Investigations

MI Hope Inc. dba Center for Complex Infectious Diseases IRB

Department of Health and Human Services

Public Health Service
Food and Drug
Administration
Silver Spring, MD 20993

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Ref: 10-HFD-45-10-02

W. John Martin, M.D., Ph.D.
MI Hope Inc. dba Center for Complex Infectious Diseases
1634 Spruce Street
South Pasadena, CA 91030

Dear Dr. Martin:

Between May 14 and 27, 2009, Ms. Diane Van Leeuwen, Mr. Babajide Osunsanmi, and Ms. Natalie Ayoub, representing the Food and Drug Administration (FDA), inspected the Institutional Review Board (IRB) at MI Hope Inc. dba Center for Complex Infectious Diseases. 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 investigations of products regulated by FDA. We are aware that at the conclusion of the inspection, our investigators 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 make IRB records, required by the regulations, accessible for inspection and copying by authorized representatives of the Food and Drug Administration at reasonable times and in a reasonable manner [21 CFR 56.115(b)].

Our inspection revealed that the IRB records are stored at the private residence of Dr. W. John Martin. FDA Investigators were not permitted access to inspect and copy IRB records at reasonable times and in a reasonable manner. Limited records were provided during the inspection, but only after lengthy delays. Access to IRB records is required to determine that IRB procedures for the protection of human subjects are adequate, and that they comply with the regulatory requirements of 21 CFR, parts 50 and 56.

2. The IRB failed to prepare and maintain a list of IRB members identified by name; earned degrees; representative capacity; indications of experience sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution [21 CFR 56.115(a)(5)].

Our inspection revealed that the IRB does not maintain a list of IRB members in compliance with the regulations. The list provided by the IRB entitled, "Individuals who have either participated or indicated their willingness to participate in the IRB meetings," fails to distinguish current IRB members, and fails to identify IRB members by representative capacity or by affiliation with the institution.

3. 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 nonscientific areas [21 CFR 56.108(c)].

As noted in citation #2 above, the IRB did not prepare and maintain a list of IRB members in accordance with the regulations and, as a result, the names and qualifications of the current IRB members cannot be confirmed. The IRB meeting minutes for January 24, 2006, indicate that the IRB unanimously approved the study entitled, **(b)(4)** with W. John Martin, M.D., Ph.D. as the Principal Investigator. The minutes list a total of twelve individuals in attendance at the meeting, including Dr. Martin, who is listed as nonvoting because of his role as Principal Investigator on the study under review. From the documents reviewed, it cannot be confirmed whether a majority of the IRB members were present at the meeting and voted to approve the noted study, and whether any individual in attendance was a nonscientist member.

In addition, the meeting minutes list three of the twelve individuals as attending the IRB meeting by proxy. In order for research to be approved at a convened meeting, the research must receive the approval of a majority of those members who are actually present at the meeting. Allowing IRB members to attend meetings by proxy is not an acceptable practice.

4. The IRB failed to prepare and maintain minutes of IRB meetings in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution [21 CFR 56.115(a)(2)].

The IRB meeting minutes of January 24, 2006, indicate that the study entitled, **(b)(4)** was approved unanimously by the IRB. Our inspection revealed that the meeting minutes are not sufficiently detailed to indicate the number of members voting for, against, and abstaining. While the meeting minutes indicate Dr. Martin was nonvoting because of his role as Principal Investigator, it is not possible to determine who voted to approve the **(b)(4)** study.

In addition, the IRB Policies and Procedures require IRB members leave the room before the discussion and voting occur on any proposal in which they have a conflicting interest. The IRB meeting minutes are not sufficiently detailed to indicate whether or not Dr. Martin left the room before the discussion and voting occurred on the study in which he had a conflicting interest.

5. The IRB failed to prepare and maintain written procedures for the IRB and failed to follow written procedures as required by 21 CFR 56.108(a) and (b) [21 CFR 56.115(a)(6)].

The IRB is required to follow written procedures in order to approve research covered by the regulations. Our inspection revealed that the IRB Policies and Procedures do not include a written procedure to address the following regulatory requirements:

a. Reporting the IRB's findings and actions to the investigator and the institution;
b. Determining which projects require review more often than annually and which projects need verification from sources other than the investigator that no material changes have occurred since previous IRB review;
c. Ensuring prompt reporting to the IRB of changes in research activity;
d. Ensuring that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate

hazards to human subjects;
e. Ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of any unanticipated problems involving risks to human subjects or others;
f. Ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of any instance of serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB;
g. Ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of any suspension or termination of IRB approval.

FDA Imposed Restrictions on the IRB:

Given the seriousness of these violations and the risk to the rights and welfare of human research subjects, the FDA is placing the following two restrictions on MI Hope Inc. dba Center for Complex Infectious Diseases IRB, per 21 CFR 56.120(b)(1) and (2):

1. No new studies subject to the requirements of 21 CFR part 56 will be approved.
2. No new subjects will be added to ongoing studies subject to 21 CFR part 56.

These restrictions will remain in effect until such time that you receive written notification from FDA that adequate corrections have been made. These restrictions do not relieve the IRB of its responsibility for receiving and responding to reports of unexpected and serious reactions and routine progress reports from ongoing studies.

Within fifteen (15) working days of receiving this letter, you are to notify the FDA of the specific actions you have taken or plan to take to bring the IRB into full compliance with FDA regulations. Your response should include any documentation necessary to show that full and adequate correction has been achieved, and should include the projected completion dates for each action to be accomplished.

It is your responsibility to notify all affected sponsors and clinical investigators of the restrictions described above. Include with your response to the FDA a representative sample copy of the IRB's written communication(s) to affected sponsors and clinical investigators, notifying them of the current restrictions. Please also provide a complete list of all sponsors and investigators who were notified as a result of this action and the date(s) on which they were notified.

Please provide a list of all studies currently being conducted that are affected by the above restrictions, and include the titles of the studies (with IDE or IND numbers, if applicable), the names of the test articles, the names of the clinical

investigators, dates of initial reviews and approvals, and the dates of continuing reviews. IND and IDE numbers can be obtained from the sponsor of the protocols affected by these restrictions.

Failure to respond to this letter and take appropriate corrective action could result in FDA taking regulatory actions, as authorized by 21 CFR 56.120, 56.121, and 56.124. These actions include, but are not limited to, the continuation of the restrictions described above, the termination of ongoing studies subject to 21 CFR part 56 and approved by your IRB, and the initiation of regulatory proceedings for disqualification of your IRB.

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 MI Hope Inc. dba Center for Complex Infectious Diseases IRB's practices and procedures comply fully with all applicable statutes and regulations.

If you have any questions, please contact Kevin Prohaska, D.O., M.P.H., at 301-796-3707; FAX 301-847-8748. Your written response and any pertinent documentation should be addressed to:

Kevin Prohaska, D.O., M.P.H.
Acting Human Subjects Protection Team Leader
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Building 51, Room 5356
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
Food and Drug Administration

cc: Dr. James Julian
IRB Chairman
MI Hope Inc. dba Center for Complex Infectious Diseases IRB
1634 Spruce Street
South Pasadena, CA 91030

Kristina C. Borror, Ph.D.
Director, Division of Compliance Oversight
Department of Health and Human Services
Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville MD 20852

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LESLIE K BALL
10/19/2009