Inspections, Compliance, Enforcement, and Criminal Investigations

Phillips, Robert A., M.D. 7/20/09

hhsbluebirdDepartment of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

JUL 20 2009

WARNING LEITER

VIA FEDERAL EXPRESS

Robert A. Phillips, M.D.
5719 Old Marion Highway
Florence, South Carolina 29506

Dear Dr. Phillips:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at your clinical site from January 20 through March 31, 2009, by investigators from the FDA Atlanta District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the **(b)(4)** study **(b)(4)** The **(b)(4)** are devices as that term is defined section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321(h). This letter also requests prompt corrective action to address the violations and discusses your written response, received on May 6, 2009, to the noted violations.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval (PMA) applications, and Premarket Notification submissions [510(k)] are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the district office revealed several violations to of Federal Human Subjects and Part 812 - Investigational Device Exemptions. At the close of the inspection, the FDA investigators presented an inspectional observations Form FDA 483 for your review and discussed the observations listed on the form with you. The deviations noted on the Form FDA 483, your written response received May 6, 2009, and our subsequent review of the inspection report, are discussed below:

1. Failure to ensure that informed consent was obtained in accordance with 21CFR Part 50. 21 CFR 812.100.

An investigator is responsible for ensuring that informed consent is obtained in accordance with 21 CFR Part 50. 21 CFR 812.100. No investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.**1** 21 CFR 50.20. You failed to ensure that informed consent was obtained from all individuals participating in the study. Examples of these failures include, but are not limited to, the following:

No records are available that document you obtained informed consent from the following individuals prior to treating them with the investigational device:

a. **(b)(6)** was **(b)(6)** the investigational device on 9/21/06.

b. **(b)(6)** was **(b)(6)** the investigational device on 4/6/06.

Your written response states that during the procedure you were given the investigational device as opposed to the standard **(b)(4)** device and were told at that time that no standard **(b)(4)** devices were available. In addition, you stated that you are certain that all consents were obtained before any procedures were performed. Your response is inadequate as it lacks a corrective and preventive action plan to ensure that adequate informed consent forms are provided to study participants prior to any study related procedures in the future. Please provide copies of policies and procedures that you have developed and implemented to ensure that adequate consent forms are provided to study subjects prior to any study related procedures. In addition, please maintain documentation that ensures that all applicable study personnel have reviewed these policies and procedures.

2. Failure to obtain IRB approval prior to requesting the written informed consent of any subject and allowing any subject to participate in an investigation. 21 CFR 812.110(a).

An investigator may determine whether potential subjects would be interested in participating in an investigation, but shall not request the written informed consent of any subject to participate, and shall not allow any subject to participate before obtaining IRB and FDA approval. 21 CFR 810.110(a). You failed to adhere to this regulation. The IRB approved your study on **(b)(4)**. At that time, the IRB notified you that the approval would expire on **(b)(4)** and informed you that it was your responsibility to request an annual renewal. You failed to request a renewal as required and allowed the IRE approval to expire on **(b)(4)**. However, even after IRE approval had expired, you still obtained informed consent from Subject **(b)(6)** and **(b)(4)** the subject using the investigational device on **(b)(4)**

3. Failure to conduct an investigation in accordance with the investigational plan [21 CFR 812.110(b)].

An investigator shall conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA. 21 CFR 812.110(b). You failed to adhere to this regulation. For

example, the protocol states that **(b)(4)** However, you reported the death of subject **(b)(6)** who expired on **(b)(6)** to the sponsor almost two years later on **(b)(4)**.

Your written response states that this was an oversight which you have corrected, however; your response is inadequate because it does not provide any corrective or preventive actions to ensure that this violation does not recur. In your response to this letter, please provide us with your corrective action plan.

4. Failure to maintain accurate, complete, and current records of receipt, use, or disposition of a device and records of each subject's case history and exposure to the device [21 CFR 812.140(a)(2)(i) and 21 CFR 812.140(a)(3)].

As an investigator, you are responsible for maintaining accurate, complete, and current records related to your participation in an investigation, including the receipt, use, or disposition of a device that relate to the type and quantity, dates of receipt, batch number or code mark. 21 CFR 812.140(a)(2)(i). You are also required to maintain records of each subject's case history and exposure to the device. 21 CFR 812.140(a)(3). Examples of your failure include, but are not limited to, the following:

i. Your site enrolled **(b)(4)** subjects, however your device accountability log indicates that **(b)(4)** devices were received and only **(b)(4)** subjects appear to have been **(b)(4)** with the investigational device.

ii. Documents obtained from the sponsor show that **(b)(4)** devices were shipped to your site. One device was defective, and **(b)(4)** devices were used. **(b)(4)** devices remain unaccounted for.

Your written response states that although the sponsor did not inform you that device accountability was your responsibility, you are now aware that these records must be maintained by your office. In addition, your written response states that all devices have been accounted for during a recent sponsor audit. Your response is incomplete. Please provide your corrective and preventive actions to ensure you maintain accurate, complete, and current records of device accountability in the future.

5. Failure to submit progress reports on the investigation to the sponsor, the monitor and the reviewing IRB at regular intervals, but in no event less often than yearly [21 CFR 812.150(a)(3)].

As an investigator. you are responsible for submitting progress reports to the reviewing IRE at regular intervals, but in no event less often than yearly. 21 CFR 812.150(a)(3). You failed to adhere to the above stated regulation in that you failed to submit any annual report to the IRB after the IRB's approval of the investigation. The sponsor inquired about the annual renewal of the study on **(b)(4)** in which the IRB, according to their records, stated the study had expired on **(b)(4)** As a result, the IRB informed you on **(b)(4)**, that due to the expiration, the study was non-compliant for continuing review and that the study was temporarily suspended.

Your written response states that you were not aware that annual reports were required and that

the IRB coordinator reviewed your studies annually without an annual report. Your response is inadequate because it does not provide your corrective and preventive actions for reporting to the IRB and the sponsor. Please provide your corrective and preventive actions to ensure prompt reporting.

The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical study. It is your responsibility as a clinical investigator to ensure compliance with the Act and applicable regulations.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in future studies for which you are the clinical investigator. In addition, please provide a complete list of all clinical trials in which you have participated for the last five years, including the name of the study and test article, the name of the sponsor, the number of subjects enrolled, and the current status of the study. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA 812.119.

You will find information to assist you in understanding your responsibilities and planning your corrective actions in the FDA Information Sheets Guidance for Institutional Review Boards and Clinical Investigators, which can be found at http://www.fda.gov/oc/ohrt/irgs/. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Sent your response to: Attention: Anne Hawthorn, J.D., Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 10903 New Hampshire Avenue, Building 66, room 3504, Silver Spring, Maryland 20993-0002.

A copy of this letter has been sent to the Atlanta District Office, 60 Eighth Street, NE, Atlanta, Georgia 30309. Please send a copy of your response to that office.

If you have any questions, please contact Anne Hawthorn, J.D., (301) 796-6561, anne.hawthom@fda.hhs.gov.

Sincerely yours,

/S/

Timothy A. Ulatowski

Director
Center for Devices and
Radiological Health

cc: **(b)(6)**

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1 The exceptions for this general requirement to obtain informed consent are enumerated in 21 CFR 50.23 and 21 CFR 50.24.