

# Inspections, Compliance, Enforcement, and Criminal Investigations

**Ward, John A., M.D. 12/03/09**



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-45-12-01

John A. Ward, M.D.  
Capstone Clinical Trials, Inc.  
2018 Brookwood Medical Center Drive, Suite 314  
Birmingham, AL 35209-6870

Dear Dr. Ward:

Between May 12 and May 20, 2009, Ms. Patricia Smith, representing the Food and Drug Administration (FDA), conducted an investigation and met with you to review your conduct of a clinical investigation [Protocol **(b)(4)** entitled **(b)(4)** of the investigational drug **(b)(4)** performed for **(b)(4)**

This inspection is a part of the FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research and to ensure that the rights, safety, and welfare of the human subjects of those studies have

been protected.

From our review of the establishment inspection report, the documents submitted with that report, and your July 17, 2009, written response to the Form FDA 483, Inspectional Observations, we conclude that you did not adhere to the applicable statutory requirements and FDA regulations governing the conduct of clinical investigations and the protection of human subjects. We are aware that at the conclusion of the inspection, Ms. Smith presented and discussed with you Form FDA 483, Inspectional Observations. We wish to emphasize the following:

**1. You failed to ensure that the investigation was conducted according to the investigational plan [21 CFR 312.60].**

The protocol required that randomization take place following screening on Day 0, one day prior to surgery. However, subjects at your site were randomized postoperatively, as opposed to preoperatively, in violation of the protocol. In a Protocol Deviations report dated May 30, 2007, your site notified the Institutional Review Board (IRB) that subjects 5001 through 5139 were randomized post-surgery.

In addition, subjects' progress notes revealed that after May 30, 2007, you continued to authorize randomization of subjects post-surgery. Examples include, but are not limited to, Subjects 5205, 5209, 5212, 5215, 5223, and 5229.

In your July 17, 2009, response to the Form FDA 483, Inspectional Observations, you stated that after receiving clarification from the sponsor on May 11, 2007, your site randomized subjects pre-surgery, many on the same day as surgery, but preoperatively. You proposed that during future studies, your site would randomize subjects as required by the protocol, and would work more closely with the sponsor to correct any perceived ambiguities. We do not find your response to be acceptable in addressing this matter. We note that you have not provided any documentation to support your statement that the subjects were randomized preoperatively after May 11, 2007.

**2. You failed to ensure that an Institutional Review Board (IRB) that complies with the requirements set forth in 21 CFR Part 56, was responsible for the initial and continuing review and approval of the clinical study [21 CFR 312.66].**

You continued to perform research activities during periods of time when IRB approval had expired. Initial IRB approval for Protocol **(b)(4)** was granted on May 31, 2006, and continued for twelve consecutive months, with an expiration date of May 31, 2007. On June 18, 2007, you submitted the Investigator's Annual Report Review to the IRB; however, IRB approval was not granted until July 2, 2007. The following 47 subjects participated in research study activities including, but not limited to, screening, dosing, and study procedures between May 31, 2007, and July 02, 2007, when IRB approval had lapsed: Subjects 5109, 5126, 5127, 5128, 5129, 5130, 5131, 5132, 5133, 5135, 5136, 5137, 5138, 5139, 5140, 5141, 5142, 5143, 5144, 5145, 5146, 5147, 5148, 5149, 5151, 5152, 5154, 5155, 5156, 5157, 5158, 5159, 5160, 5161, 5162, 5163, 5164, 5165, 5166, 5167, 5168, 5169, 5170, 5171, 5172, 5173, and 5174.

In your July 17, 2009, response to the Form FDA 483, Inspectional Observations, you stated that the lapse in IRB approval was the error of a staff member and that it was self-identified and self-acknowledged. We acknowledge your assurance that corrective actions have been taken to prevent this observation during future studies.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical study of an investigational drug. It is your responsibility to ensure adherence to each requirement of the law and relevant FDA regulations. You should address these deficiencies and establish procedures to ensure that any ongoing or future studies will be in compliance with FDA regulations.

Within fifteen (15) working days of your receipt of this letter, you should notify this office in writing of the actions you have taken 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

Building 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

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This is a representation of an electronic record that was signed electronically and  
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/s/

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LESLIE K BALL  
12/03/2009