Inspections, Compliance, Enforcement, and Criminal Investigations

Nemechek Do Pa, Patrick

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville, MD 20852-1448

June 28, 2010

By Certified Mail - Return Receipt Requested
And By Facsimile Transmission

CBER -10-06

Warning Letter

Patrick Nemechek, D.O., PA
8101 W. 135th Street
Overland Park, Kansas 66223

Dear Dr. Nemechek:

This letter describes the results of a Food and Drug Administration (FDA) inspection that was conducted from February 22 through March 22, 2010. The FDA investigators, met with you to review your conduct of the following clinical study: **(b)(4)** This inspection was conducted as part of the FDA's Bioresearch Monitoring Program, which includes inspections designed to review the conduct of research involving investigational drugs and to ensure that the rights, safety, and welfare of the human subjects of these studies have been protected.

At the end of the inspection, a Form FDA 483, Inspectional Observations, was issued and discussed with you. From our review of the establishment inspections report, and the documents submitted with the report, we have determined that you violated regulations governing the proper conduct of clinical studies involving investigational drugs, as published in Title 21, **Code of Federal Regulations** (CFR), Parts 312 and 50 (available at http://www.gpoaccess.gov/cfr/index.html[1]).

The applicable provisions of the CFR are cited for each violation listed below. We wish to emphasize the following:

1. You failed to ensure that the investigation was conducted according to the signed investigator statement and the investigational plan. [21 CFR § 312.60].

A. Of the seventeen subjects you enrolled in the study, seven did not meet the enrollment eligibility criteria set forth in the protocol, as described below:

Subject #	Date consent signed	Vaccination Date	Comments	Inclusion/Exclusion Criteria

(b)(6)	5-25-07	6-20-07	Subject had previous diagnosis of chronic hepatitis C virus infection.	Negative antibody to hepatitis C virus (anti-HCV) required for inclusion.
(b)(6)	5-30-07	6-20-07	Subject had a screening CD4 count of 537 during the screening visit.	Exclude if CD4 cells 350 ^{3} 500/ml (Group 2a).
(b)(6)	5-30-07	6-20-07	Subject was on antiretroviral therapy (ARV) for 5 months prior to screening and enrollment.	On stable ARV for greater than 6 months prior to enrollment required for inclusion.
(b)(6)	7-11-07	3-13-08	Subject had a detectable viral load greater than 400 copies at both screening and complete rescreening visits.	Viral load less than 400 copies for subjects on ARV therapy required for inclusion.
(b)(6)	1-29-08	2-20-08	Subject was enrolled on 2-20-08 with a viral load of 640 copies on 08-17-07 a viral load of 640 copies on 08-17-07 and 9-17-07.	Subjects are required to maintain viral a viral load of 640 copies on 08-17-07 greater than six months.
(b)(6)	2-19-08	4-10-08	Subject had a past medical history of *myocardial infraction* in 02-07.	Exclusion criteria #10: History of *Myocardial infarction*.
(b)(6)	2-27-08	3-19-08	Subject had a serum glucose result that was below normal limits at screening.	Inclusion Criteria Group 2 # 6: Serum glucose within normal institutional limits.

B. The protocol-required viral load count was not performed for Subject **(b)(4)** at visit 4.

C. The protocol-required urine pregnancy test was not performed for Subject **(b)(4)** at visit 5.

D. Section 4.2 of the protocol, inclusion criteria for HIV infected subjects, requires HIV-1 infection documented by **(b)(4)** and confirmed by **(b)(4)** prior to study entry. However, you failed to document the HIV infection of Subject **(b)(4)** prior to study entry.

2. You failed to ensure that informed consent was obtained in accordance with 21 CFR Part 50. [21 CFR § 312.60].

A. A letter from your reviewing IRB dated 12-3-2007 instructed you to use the updated IRB-stamped consent forms and to reconsent all current and any new prospective subjects. The consent forms were updated to implement protocol amendment #5. You obtained informed consent using an obsolete consent form from the following seven subjects, at the time of their follow-up visits.

B.

Subject #	Signature Date of Informed Consent	Informed Consent Deficiency
(b)(6)	12-13-07	Failed to use the current version of the informed consent form dated 11-26-07.
(b)(6)	12-13-07	Failed to use the current version of the informed consent form dated 11-26-07.
(b)(6)	02-19-08	Failed to use the current version of the informed consent form dated 11-26-07.

(b)(6)	2-26-08	Failed to use the current version of the informed consent form dated 11-26-07.
(b)(6)	2-27-08	Failed to use the current version of the informed consent form dated 11-26-07.
(b)(6)	2-27-08	Failed to use the current version of the informed consent form dated 11-26-07.
(b)(6)	4-24-08	Failed to use the current version of the informed consent form dated 11-26-07.

C. You obtained informed consent from Subjects **(b)(6)** and **(b)(6)** with the version of the informed consent form intended for HIV positive individuals. However, these subjects were enrolled in the study as non-HIV positive subjects with or without previous **(b)(4)** vaccination in group 1. The subjects signed the wrong consent form on 1-30-08 and 5-25-07, respectively.

3. You failed to retain records required to be maintained for the period of two years following the date a marketing application is approved for the indication for which the drug is being investigated; or, if no application is filed or if the application is not approved for such indication, until two years after the investigation is discontinued. [21 CFR § 312.62(c)].

At the time you signed the Form FDA 1572, Statement of Investigator, for the study, you agreed to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make these records available for inspection in accordance with 21 CFR 312.68. However, during the inspection, you stated that the source documents were not available because the computer "crashed." You also stated that the study data were not entered into the case report form directly. We request that you explain your corrective action plan for maintaining study records in the future.

This letter is not intended to contain an all-inclusive list of deficiencies in your clinical study of investigational drugs. It is your responsibility as the clinical investigator to ensure adherence to each requirement of the law and applicable regulations, and to protect the rights, and welfare of subjects under your care.

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 current or future studies for which you are the clinical investigator. Failure to respond to this letter and to take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. This could include the initiation of disqualification proceedings in accordance with 21 CFR 312.70.

Please send your written response to:

Solomon Yimam
Division of Inspections and Surveillance (HFM-664)
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Suite 200N
Rockville, Maryland, 20852-1448
Telephone (301) 827-1948

We also request that you send a copy of your response to the FDA office listed below.

Sincerely,
/S/
Mary A. Malarkey, Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: John Thorsky, Director
Kansas City District Office
Food and Drug Administration
11510 West 80th Street
Lenexa, Kansas 66214-3340

Links on this page:

1. http://www.gpoaccess.gov/cfrlindex.html