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Rockville MD 20852-1448

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CBER – 05--013

Warning Letter

MAY 13 2005

Janet Lowther
Gulf Coast Regional Blood Center
1400 LaConcha Lane
Houston, Texas 77054

Dear Ms. Lowther:

This letter describes the results of a Food and Drug Administration (FDA) inspection that was conducted from January 10 through January 14, 2005. FDA investigators Lillie Young and Patrick Stone met with you to review your conduct of a clinical study entitled

██████████ FDA conducted this inspection under the agency's Bioresearch Monitoring Program that includes inspections designed to review the conduct of research involving investigational devices.

At the end of the inspection, a Form FDA 483, Inspectional Observations, was issued and discussed with you. We received and reviewed your written response to the Form FDA 483, dated January 28, 2005, addressed to FDA Dallas District Director, Mr. Michael Chappell.

We have determined that you violated regulations governing the proper conduct of clinical studies involving investigational devices, as published in Title 21, Code of Federal Regulations (CFR), Parts 50 and 812 (available at <http://www.access.gpo.gov/nara/cfr/index.html>). The applicable provisions of the CFR are cited for each violation listed below.

1. **You failed to protect the rights, safety, and welfare of the subjects under your care, and you failed to ensure that the investigation was conducted according to the investigational plan, the signed agreement, and applicable FDA regulations, including Part 50. [21 CFR § 812.100].**
 - A. Protocol sections 8.0 and 9.0 require that enrolled subjects be between 18 and 55 years of age. You failed to document that 156 subjects you

enrolled in the study met these age enrollment criteria. During the inspection, your Human Resource Director sent an email to each of the 156 enrolled subjects requesting their date of birth. Review of 101 of 156 email responses showed that you enrolled at least five subjects not meeting the age requirements. Subjects [REDACTED] were enrolled although these subjects exceeded the age requirement of 55. Subject [REDACTED] was enrolled although this subject was under the age of 18 -- even though the protocol did not authorize enrollment of children in the study. In addition, age could not be verified for the following seven subjects: [REDACTED]

In your letter, you agree "that birth date information had not been obtained on the study participants." You also note that efforts continue to obtain additional confirmations of birth date and as of January 25, 2005, you had obtained an additional 28 responses. You do not state if these additional 28 subjects met the age enrollment criteria. You also state you plan to conduct a review of current processes in place in the clinical trials laboratory related to the management of clinical trial protocols. On completion of this review, you will create a method of documenting the requirements stated in the protocol. You "anticipate that this documentation process will follow the protocol and related material through the internal review, IRB review, and Quality Assurance Department review." This multi level review process should ensure that consensus is achieved regarding all protocol requirements. Your proposed corrective action, if implemented, appears to be adequate.

- B. Protocol section 10.0 and the [REDACTED] Clinical Trial Subject Information and Consent Form do not provide for the recall of subjects for additional testing. Instead, the protocol states, "With the participant still available, compare the capillary result to the whole blood result. If they are not the same, retest the whole blood in duplicate and obtain a second capillary result and test in duplicate." Subject [REDACTED] had discordant test results, but you did not collect a second finger stick sample at the initial visit for duplicate testing, as the protocol required. You asked the subject to return for a second visit and repeated both the finger stick and venipuncture without obtaining informed consent. According to the comment on the [REDACTED] Results form the "donor will be repeated because the donor left prior to test completion."

Subject	Date	FS	WB	P	S	Discordant	Comments
[REDACTED] Initial: Repeat for discordance only:	12/22/03	NR	R NR/NR	NR	NR	YES	Second finger stick not done as per protocol
[REDACTED] Initial:	12/23/03	NR	NR	NR	NR	NO	

We note that in your final report dated 2/18/04 to the IRB Chair, you provide a different explanation for repeating the entire procedure for subject [REDACTED]. You state the discordant results “were unusual in that the positive indicator line extended only halfway across the testing device. Review of this donor’s history indicated two (2) fingersticks were performed initially because the donor was not bleeding. A digital picture of the test result was sent to the study sponsor who agreed the visual observation was unusual.”

This violation was not included on the Form FDA 483.

- C. According to protocol section 13.0 an [REDACTED] representative will visit each site and train personnel according to a standardized procedure.” The [REDACTED] Clinical Trial Training Log and a memo to you dated 1/6/2005 document that [REDACTED] from [REDACTED] performed training on 12/5/03. However, your records indicate that [REDACTED] received training on 12/12/03, not 12/5/03, and do not report the identity of the trainer, or that the trainer was an [REDACTED] representative. [REDACTED] is listed as the operator performing quality control testing on 7 of 8 testing days, involving 154 subjects’ tests. In addition, there is no record of [REDACTED] on the training log or record of proficiency panel testing. Nevertheless, [REDACTED] is listed under “Performed fingerstick and testing” on the SDS [REDACTED] Summary of Responsibilities. In fact, you listed only three employees as performing testing on your [REDACTED] Summary of Responsibilities.” Only one of those employees identified on that record was also identified on the training log on the date an [REDACTED] representative was at your facility.

This violation was not included on the Form FDA 483.

- D. Protocol section 10.0 directs that “Samples will be shipped to the [REDACTED] [REDACTED] daily.” Review of the specimen shipping forms shows that you failed to ship at least 38 samples to the central laboratory on the day they were obtained. Delays in shipping ranged from two to seven days.

In your letter you agree that you failed to ship 33 of the 38 samples daily due to a “lack of oversight caused by a shortage of shipping documents” and due to “shipping over the holiday period” of 12/29/03 through 1/7/04. You initially reported that an original shipment of 5 of the 38 samples was sent on the same day as collection, but was returned from the shipping company over the Christmas holiday. Upon request of the sponsor, these returned samples were shipped again at a later date. According to your Final Report dated 2/18/04, you stated “six participants were withdrawn

from the study due to the return of one of the shipment boxes to Gulf Coast from [REDACTED]. You state in future studies you will ensure you have an adequate supply of the proper forms and will evaluate the shipment of samples over a holiday period. Your proposed corrective action appears to be adequate.

2. You failed to maintain accurate and complete records of each subject's case history, including data on the condition of each subject upon entering, and during the course of, the investigation and you failed to maintain accurate, complete and current records relating to the receipt, use, and disposition of devices. [21 CFR §§ 812.140(a)(2) and (3)].

- A. As described in item 1.A above, you failed to document that the 156 enrolled subjects met the enrollment age criterion.

As noted in your response to item 1.A above, you acknowledge you failed to maintain accurate and complete case histories of your subjects. In your letter you state that for future studies "the protocols will be reviewed at several points for requirements and documentation of these requirements. If found, deficiencies of documentation materials will be reported to the sponsor for resolution prior to implementation. Lacking resolution, the study will not be performed at this site." If you implement this procedure, your proposed corrective action appears to be adequate.

- B. You failed to maintain adequate device accountability records. There were no records documenting date and quantity of devices received. According to a copy of your device return form, you used 624 devices for subject testing and 24 devices for control testing. According to your records documenting subject test results, control test results, and proficiency panel results, the total number of devices used is 678. These records show a discrepancy of 30 devices.

Devices used for testing:	Lot #	Lot # Not Recorded	TOTAL	Documentation
Subjects	630			[REDACTED] Results Forms
Controls	24			[REDACTED] Controls Forms
Proficiency Panels		24		Proficiency Panel Results
Totals	654	24	678	

This violation was not included on the Form FDA 483.

- C. The study records included preprinted labels to insure informed consent forms and blood samples would be assigned a unique participant number. However, it appears one number was assigned to two participants. Upon review of the [REDACTED] Results' Forms, it is noted that two preprinted labels, both [REDACTED] were placed on two different pages. Both pre-printed labels are under the category "Participant #" and both subjects were tested on 12/22/03. One [REDACTED] entry is initialed and dated 12/30/03 with the following changes noted: a line placed through the [REDACTED] and a handwritten number of [REDACTED]. Please explain this use of duplicate preprinted labels.

This violation was not included on the Form FDA 483.

This letter is not intended to contain an all-inclusive list of deficiencies in your clinical study of investigational devices. 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, safety, and welfare of subjects under your care.

You should notify this office, in writing, within fifteen (15) business days of receipt of this letter, of the steps you plan to implement to prevent the recurrence of similar violations in future studies. Your response should include any documentation necessary to show that correction has been achieved.

This Warning Letter is issued to you because of the serious nature of the observations noted at the time of the FDA inspection. Please be advised that failure to implement effective corrective actions and/or the commission of further violations may result in the initiation of enforcement action(s) without further notice. These actions could include injunction and initiation of clinical investigator disqualification proceedings, which may render you ineligible to receive investigational devices.

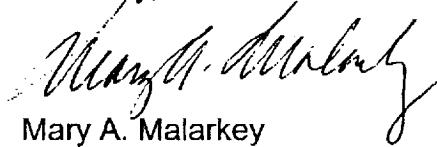
Please send your written response to:

Janet K. White
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) 827-6339

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

Sincerely,



Mary A. Malarkey
Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: Michael A. Chappell, Director
Dallas District Office
Food and Drug Administration
4040 North Central Expressway, Suite 300
Dallas, Texas 75204

Susan N. Rossman, M.D., Ph.D., Chair
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