DEPARTMENT OF HEALTH & HUMAN SERVICES

95068d

Food and Drug Administration

Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

NOV - 5 2004

By Certified Mail – Return Receipt Requested
And by Facsimile Transmission

CBER – 05--003

Warning Letter

Timothy W. Purington
Tapestry Health Systems
320 Riverside Drive
Florence, Massachusetts 01062

Dear Mr. Purington:

This letter describes the results of a Food and Drug Administration (FDA) inspection that was conducted from June 24 through July 6, 2004. FDA investigator Diane Thibodeau met with you to review your conduct of a clinical study entitled [redacted] *Clinical Trial – Protocol #*[redacted] 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 July 22, 2004, addressed to FDA District Director Gail Costello at the FDA New England District Office.

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), Part 50 and Part 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 and the signed agreement. [21 CFR § 812.100].**

A. Protocol sections 8.0 and 9.0 require that enrolled subjects be between the ages of 18 and 55 and able to sustain venipuncture. Subjects with life threatening illnesses (with the exception of [redacted], as well as those with suppressed immune systems, were to be excluded from the study. You enrolled 554 subjects in the study, but you failed to document that the subjects met the enrollment criteria of health status and age. Secondary records recovered at the time of the inspection provided the date of birth for 76 of the 554 subjects. Review of the 76 retrieved records showed that you enrolled subjects [redacted] and [redacted] in the study although these subjects exceeded the age requirement for study enrollment.

In your response to the Form FDA 483, you agreed that the "inclusion/exclusion criteria was not documented per the protocol" and agreed that some subjects over 55 years of age were "erroneously enrolled".

B. You requested that four subjects return to the clinic to have a second finger stick and venipuncture. Protocol section 10.0 and informed consent forms [redacted] Clinical Trial Protocol [redacted] version 11/28/01 (Northampton) and version 12/14/01 (Springfield) ***do not provide for*** the recall of subjects for additional testing.

Subject #	Date Tested	New Subject #	Date Retested
[redacted]	2/8/02	[redacted]	2/28/02
	2/21/02		2/28/02
	2/8/02		2/28/02
	2/22/02		3/8/02

These violations were not included on the Form FDA 483.

C. Protocol section 15.0 requires that controls be run daily at a minimum. Controls were not run on the following testing days for 23 subjects at both locations.

Date	Site	Subject(s)	# of Subjects
1/3/02	Springfield	[redacted]	1
1/4/02	Springfield		3
1/11/02	Northampton		1
2/20/02	Springfield		3
3/1/02	Northampton		14
4/8/02	Northampton		1

These violations were not included on the Form FDA 483.

D. The [redacted] package insert states the following categories will be used to record interpretation of results: Reactive (R), Non-Reactive (NR), and Invalid (I).

The result "Indeterminate" ("IND") was recorded for the following subjects:

i. Subject [redacted] Two finger stick results; one whole blood result

ii. Subject [redacted] One serum result

iii. Subject [redacted] Two finger stick results
The original [redacted] results form shows the result was changed from IND to R.

Reporting the result "IND" for subjects [redacted] and [redacted] resulted in an erroneous determination of discordance between the finger stick and whole blood. As a consequence the subjects experienced a second finger stick, and excess testing not specified by the protocol was performed. The test results for subject [redacted] were excluded from the study for reasons that were not explained.

In your letter, you acknowledge "IND was not an available option within the study protocol. This was considered an operator error."

E. Protocol section 10.0 states "Samples will be sent to the [redacted] daily." Review of [redacted] Reports shows that you failed to ship the samples to the [redacted] each day for seven of eighteen records reviewed during the inspection.

Specimen #	Date collected	Date Received
[redacted]	2/8/2002	2/13/2002
	12/27/2001	1/3/2002
	12/27/2001	1/3/2002
	12/27/2001	1/3/2002
	12/27/2001	1/3/2002
	12/27/2001	1/3/2002
	12/27/2001	1/15/2002

These violations were not included on the Form FDA 483.

F. You and your staff failed to complete the required "Proficiency Panel Testing" prior to initiation of subject study testing. You enrolled and tested study subjects between December 2001 and March 2002, but the testing personnel did not perform the "Proficiency Panel Testing" until April 2002, after all 554 subjects were enrolled and the study was completed.

Furthermore, two individuals listed on your Clinical Trial Training Log did not perform proficiency testing at all. These two unauthorized individuals performed control testing on numerous days as listed in the table below. Since your subject testing results forms do not include operator's initials, the extent of additional unauthorized testing is not known.

Individual's Initials	Control Testing Dates
[redacted]	1/11/02, 2/3/02, 2/4/02, 2/13/02, 2/27/02
[redacted]	2/5/02, 2/26/02, 3/19/02

This violation was not included on the Form FDA 483.

2. You failed to obtain informed consent in accordance with the provisions of 21 CFR Part 50.27(a). [21 CFR § 812.100].

A. The informed consent forms, versions 11/28/01 (Northampton) and 12/14/01 (Springfield), that were approved by the Institutional Review Board (IRB) on 12/28/01 were modified without IRB approval at both sites. You crossed out the word "Doctor" on the signature line and, in some instances, inserted "Counselor". This change was not reviewed and approved by the IRB. In addition, one individual signed informed consent forms for subjects [redacted] and [redacted] and was neither a doctor nor listed on the Clinical Trial Training Log.

In your response letter, you agree that you should have submitted the revised form to the IRB for review.

B. You involved human beings as subjects in this research prior to IRB approval of the informed consent form. Subjects [redacted] through [redacted] were enrolled, consented, and tested on 12/20/01 (Subject [redacted]) and 12/27/01 (Subjects [redacted]) at the Springfield site. The informed consent form was approved by the IRB on 12/28/01.

In your letter, you agree with this observation.

3. **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. [21 CFR § 812.140(a)(3)(ii)].**

A. As described in item 1.A above, you failed to document that the 554 enrolled subjects met the enrollment criteria of health status and age.

In your letter, you agreed that these inclusion/exclusion criteria were not documented.

B. The informed consent forms signed by subjects [redacted] through [redacted] at the Springfield site were not available for review during the inspection.

During the discussion at the end of the inspection and in your letter, you explained that these consent forms have been "temporarily misplaced," possibly during a recent office move. You also noted that you will notify FDA when these documents are located. To date, we have not received such notification from you.

This letter is not intended to contain an all-inclusive list of deficiencies in your clinical studies 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 new 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) 827-6221

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

Sincerely,

James S. Cohen, J.D.
Acting Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: Gail T. Costello
District Director, HFR-NE200
Food and Drug Administration
One Montvale Ave., 4th Floor
Stoneham, Massachusetts 02180

[redacted] M.D., Chair
[redacted]