



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

95178d

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

AUG 25 2005

By Certified Mail – Return Receipt Requested
And by Facsimile Transmission

CBER – 05--028

Warning Letter

Steven Peltzman, CEO
Saliva Diagnostic Systems, Inc.
1 Clark Hill Road
Framingham, Massachusetts 01701

Dear Mr. Peltzman:

This letter describes the results of Food and Drug Administration (FDA) inspections of [redacted] clinical investigators on your study entitled *Saliva Diagnostic Systems, Inc. (SDS) Hema-Strip™ HIV Clinical Trial -- Protocol #03-HIV01*, and of [redacted]

[redacted] The inspection of [redacted] was conducted from [redacted] by FDA investigators M. Patricia Murphy and Karen McNabb-Noon. The clinical investigators, trial sites and codes, FDA investigators, and dates the inspections were conducted are shown in the table below. FDA conducted these inspections under the agency's Bioresearch Monitoring Program, which includes inspections designed to review the conduct of research involving investigational devices.

Clinical Investigator	Trial Site(s)	Site Code	FDA Investigator(s)	Dates of Inspection
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[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
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At the end of the inspections, a Form FDA 483, Inspectional Observations, was issued and discussed with [redacted], President, and [redacted], Vice President, of [redacted]

[REDACTED]
Copies of the Form FDA 483 for all [REDACTED] inspections are enclosed for your information.

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 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 ensure proper monitoring of the investigation.
[21 CFR § 812.40].**

A. In your investigational plan submitted to the FDA as part of your IDE application, you [REDACTED] and according to section [REDACTED] you agreed to do the following: 1) monitor each site regularly throughout the study, 2) perform quality control testing on a daily basis, 3) conduct training at each site, 4) conduct the study in accordance with the study protocol, and 5) assure that all records and required reports were accurate, complete and current. All [REDACTED] of the inspections disclosed violations, described below, so numerous and pervasive that they demonstrate that you failed to properly monitor the study.

- 1) All [REDACTED] sites enrolled ineligible subjects, [REDACTED] and failed to document that all of the subjects enrolled met the inclusion criteria of health status and/or age and/or having medical documentation available to confirm their positive HIV status as required by protocol sections [REDACTED] and [REDACTED].
- 2) Repeat testing was conducted on two subjects [REDACTED] and [REDACTED], in violation of protocol section [REDACTED] and the informed consent form signed by the subjects.
- 3) Two sites failed to run controls at least daily, as required by protocol section [REDACTED], for [REDACTED] subjects on [REDACTED] testing days [REDACTED] and for [REDACTED] subjects on [REDACTED] testing days [REDACTED].
- 4) All [REDACTED] sites failed to send samples to the central reference laboratory daily as required by protocol section [REDACTED] for at least [REDACTED] [REDACTED] specimens collected.
- 5) Three sites [REDACTED] failed to have testing personnel complete the "Proficiency Panel Testing" prior to initiation of subject study testing, as required by the investigational plan.
- 6) At least two sites [REDACTED] also deviated from protocol section [REDACTED] and FDA regulations by failing to [REDACTED].

- [REDACTED]
- 7) The sites 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. As described in item A.1) above, the sites failed to document that the [REDACTED] enrolled subjects at the [REDACTED] sites met the enrollment criteria as required by the protocol.
 - 8) Two sites [REDACTED] failed to document temperatures for the test kits received at their sites showing proper storage of the investigational device as required by the protocol, Appendix VI: Package Insert.

B. Monitoring reports were inaccurate. After auditing the clinical sites [REDACTED] [REDACTED] reported "no issues occurred during the study" regarding health status inclusion criterion, testing done in accordance with the study protocol and forwarding samples to the reference laboratory at all [REDACTED] sites. [REDACTED] also reports "all control data was reviewed and there are no deviations." [REDACTED] did not report any device accountability discrepancies or investigational storage requirements not being met. In fact, as described in 1.A. above, these reports were inaccurate.

C. There were inconsistencies between the source documents prepared by the investigators (the SDS Results Forms, Control Forms, Training Forms, and Discordances) and the data submitted to the FDA.

2. You failed to use monitors qualified by training and experience. [21 CFR § 812.43(d)].

Two of the [REDACTED] monitors for the sites appear not to have had any experience in compliance with FDA regulations governing clinical trials prior to their employment at [REDACTED]. One monitor's position prior to this was for a manufacturing company where she worked in areas unrelated to clinical trials. This monitor provided a single day of training to another individual, who apparently worked only part time as an [REDACTED] monitor. Her regular position is [REDACTED]. There is no documentation that either had any training in applicable FDA regulations.

3. You failed to submit a complete IDE application to FDA, failed to ensure that FDA was promptly informed of significant information about an investigation, and began part of an investigation before FDA approved the supplemental application. [21 CFR §§ 812.20(b)(4),(7), 812.40, and 812.42].

You advised FDA in your last submission, dated [REDACTED] that you were "recruiting study sites" and the site principal investigators were "to be determined."

Your IDE application was incomplete because you failed to identify any institutions participating in the investigation. You never notified the FDA of this significant information and you began this part of the investigation before receiving FDA approval.

**4. You failed to prepare and submit a current investigator list.
[21 CFR § 812.150(b)(4)].**

You failed to submit a current list of the names and addresses of all investigators participating in the investigation to the FDA. This list is to be provided at 6-month intervals, submitting the first such list 6 months after FDA approval. According to section [REDACTED] of the last IDE submission, dated [REDACTED] [REDACTED] you are "presently recruiting study sites." The studies started December 10, 2003 and ended March 30, 2004. There was no submission providing a list of principal investigators to the FDA.

Several of the items listed above are described in the five enclosed warning letters: [REDACTED]

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 sponsor 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.

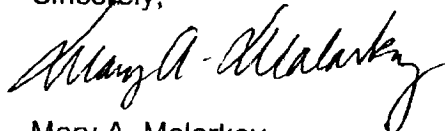
Please send your written response to:

Janet K. White
Division of Inspections and Surveillance (HFM-664)
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
1401 Rockville Pike, Suite 200N
Rockville, Maryland, 20852-1448
Telephone: (301) 827-6339

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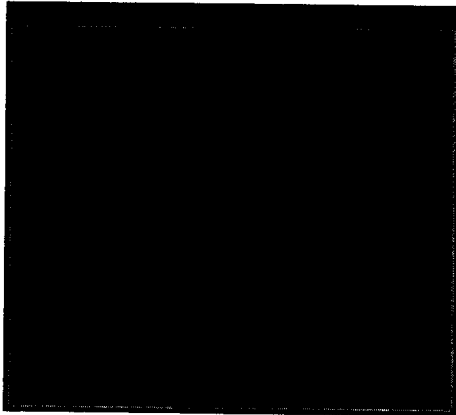
We request that you send a copy of your response to the FDA District Office listed below.

Sincerely,



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

Enclosures:



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