DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

FEB 24 2005

Via Federal Express

WARNING LETTER

Trent Nichols, M.D.
Advanced Magnetic Research Institute - Pennsylvania
195 Stock Street, Suite 211b
Hanover, Pennsylvania 17331

Dear Dr. Nichols:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site. Ms. Susan Laska, an investigator from the FDA's Philadelphia District Office, conducted the inspection from November 16 through November 22, 2004. The purpose of the inspection was to determine if your activities and procedures as a clinical investigator for the [redacted] studies sponsored by [redacted] complied with applicable FDA regulations. The [redacted] is a device as that term is defined under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), because it is intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, or because it is intended to affect the structure or any function of the body.

The FDA conducted the inspection under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval Applications (PMA), or Premarket Notification [510(k)] submissions are scientifically valid and accurate. The program also ensures that human subjects are protected from undue hazard or risk during scientific investigations.

Our review of the inspection report submitted by the Philadelphia District Office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR), Part 812 – Investigational Device Exemptions, and Part 50-Protection of Human Subjects, and Section 520(g) of the Act . At the close of the inspection, Ms. Laska presented a Form FDA 483 "Inspectional Observations" to you for review and discussed the listed deviations. The deviations noted on the Form FDA 483 and our subsequent inspection report review are discussed below:

Failure to provide adequate informed consent (21 CFR 812.100 and 21 CFR 50.20, 50.25, and 50.27(a)).

Pursuant to 21 CFR 812.100, an investigator is responsible for ensuring that informed consent is obtained from each subject in accordance with 21 CFR Part 50. In accordance with 21 CFR 50.20, "no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative." The informed consent shall be documented by the use of a written consent form that embodies the elements of informed consent required by 21 CFR 50.25. This form must be approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. (21 CFR 50.27(a)). Examples of your failure to comply with the informed consent requirements include but are not limited to the following:

- The informed consent document used to obtain consent from subjects enrolled in the study lacked the following required elements:
    - an explanation of alternative procedures, if any, that might be advantageous to the subjects;
    - a description of any reasonably foreseeable risks or discomforts to the subjects; and
    - a description of any benefits to the subjects that may be reasonably expected from the research.

- There is no documentation to show that the informed consent form used in the study during the period of 2003 and 2004 was ever reviewed and approved by an IRB.

- Study subjects were not provided with a copy of the informed consent form.

Failure to ensure that the investigation is conducted according to the signed agreement, the investigational plan, applicable FDA regulations, and any conditions imposed by the IRB (21 CFR 812.100 and 812.110(b) and (c)).

A clinical investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations. (21 CFR 812.100). In addition, the clinical investigator shall conduct an investigation in accordance with any conditions of approval imposed by an IRB or the FDA (21 USC 812.110(b)). Your failure to adhere to these regulations includes but is not limited to the following:

- Preliminary diagnostic tests such as EKG, blood chemistries, and imaging or other physiologic studies were not completed as specified in the protocol, which is part of the investigational plan (21 CFR 812.25(b)). Also, the protocol for the [redacted] in the [redacted] study specified a neurometer be used for performing nerve conduction test. Nerve conduction tests were not completed for the subjects in the [redacted] study.

- Forms required by the protocol such as the initial contact and exclusion forms, demographic form, pre-treatment check sheet, session check time form, or disease specific questionnaire were not found in any of the charts reviewed.

- Review of the study records revealed that 3 subjects ([redacted], and [redacted]) were treated with the device, yet there is no documentation that these subjects were seen and evaluated by Dr. Nichols. FDA regulations provide that an investigator shall permit an investigational device to be used only with subjects under the investigator's supervision. An investigator shall not supply an investigational device to any person not authorized to receive it. (21 CFR 812.110(c)).

Failure to maintain accurate, complete, and current records relating to the investigator's participation in the investigation. (21 CFR 812.140(a)).

Pursuant to 21 CFR 812.140(a), a clinical investigator must maintain accurate, complete, and current records relating to the investigator's participation in an investigation. Your failure to satisfy these requirements includes but is not limited to the following:

- There is no file maintained that includes correspondence with the IRB and the sponsor regarding actual approval of study protocols, informed consent, periodic reports, and submission/approval of advertisements of the investigational [redacted] device. A specific example related to the advertisement includes an advertisement that was run in a local central Pennsylvania magazine recruiting subjects. There is no documentation that this advertisement was ever submitted to the IRB for approval.

- Records of exposure to the device, including the date and time of each use, were not completed for all subjects. For example, there is no documentation of device exposure time for subjects [redacted] and [redacted]

The above described deviations are not intended to be an all-inclusive list of deficiencies that may exist in this clinical study. It is your responsibility as a clinical investigator to ensure that you adhere to applicable FDA regulations.

Within fifteen (15) working days after receiving this letter please provide written documentation of the additional specific steps you have taken or will take to correct these violations and prevent the recurrence of similar violations in current and future studies. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings against you in accordance with 21 CFR 812.119.

In addition to the above, we are concerned that you participated as a voting member of the IRB that reviewed your study. The Meeting Minutes from the [redacted] meeting held on 01/21/99 reveal that you were elected president of the IRB and voted on research regarding the [redacted] study. You also participated and voted on issues regarding the [redacted] study during the IRB meetings held on 1/28/01, 1/18/02, 2/1/03, and 2/7/04.

Please send your response to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch (HFZ-312), 2094 Gaither Road, Rockville, Maryland 20850, Attention: Viola Sellman, Chief, Program Enforcement Branch.

We are also sending a copy of this letter to FDA's Philadelphia's District Office, US Customhouse, Room 900, 2nd & Chestnut Street, Philadelphia, Pennsylvania 19106. We request that you also send a copy of your response to that office. If you have any questions, please contact Ms. Sellman at (240) 276-0125, or by email at vxs@cdrh.fda.gov.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health