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AUG 25 2004

WARNING LETTER

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

VIA FEDERAL EXPRESS

Patrick Farrell, CEO
Henrico Doctors' Hospital
7700 East Parham Road
Richmond, VA 23294

Dear Mr. Farrell:

This Warning Letter informs you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at Henrico Doctors' Hospital Institutional Review Board (IRB) and requests a response, including additional information regarding the corrective actions you proposed in your June 8, 2004 written submission. Ms. Candice C. Mander, an investigator from FDA's Baltimore District Office, conducted the inspection from April 6 through 9, 12 through 13, and 20, 2004.

The purpose of the inspection was to determine whether your activities and procedures as an IRB complied with applicable FDA regulations. The regulations apply to your oversight of certain clinical studies of products regulated by the FDA.

Our review of the inspection report prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR) Part 56-Institutional Review Boards. At the close of the inspection, Ms. Mander 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 review of the inspection report are discussed below:

**1. Failure to prepare, maintain, and follow adequate written procedures.
(21 CFR 56.108 and 56.115(a)(6))**

FDA regulations at 21 CFR 56.115(a)(6) require the IRB to prepare, maintain, and follow written procedures for its review of research as specified in 21 CFR 56.108.

You failed to adhere to these regulations. For example, the Henrico Doctors' Hospital IRB lacked the following:

- Procedures for how the IRB will determine whether each investigation presented for IRB approval as a non-significant risk (NSR) device study involves an NSR device. Under 21 CFR 812.2(b)(1)(ii), to be eligible for

the application of abbreviated requirements, a sponsor must submit and obtain approval, as part of its application to the IRB, of an explanation as to why its device is a non-significant risk device. Under 21 CFR 56.109(a), an IRB is required to review and reach a determination about this and all other research activities covered by these regulations. As part of its initial review of research, then, the IRB must establish and follow procedures for determining whether each investigation presented for IRB approval as an NSR device study involves an NSR device.

- Procedures for the prompt reporting to the FDA of unanticipated problems involving risks to subjects; instances of serious or continuing noncompliance with FDA regulations or IRB requests; and suspension or termination of IRB approval.

In addition, the IRB failed to follow some of its own written procedures. For example:

- Although there were no progress reports on the IRB form titled, "Status Report/Request for Renewal of Approved Protocol" submitted for the following studies, the IRB did not terminate the approval of the research studies as required in the IRB's continuing review procedures.
 - a. "A Pivotal, Double-Blind, Comparative, Multicenter Study to Determine the Efficacy and Safety of [REDACTED] in the Reduction of Post-Surgical Adhesions After Laparoscopic Surgery;" and
 - b. "A Post-Approval Investigation of the [REDACTED]™ [REDACTED] / [REDACTED]™ [REDACTED] [REDACTED] [REDACTED] for Anterior Open and Laparoscopic Interbody Fusion in Patients with Symptomatic Degenerative Disc Disease."
- There was no documentation that the IRB invited clinical investigators in writing to present their protocols at the next scheduled IRB meeting as part of the initial review process, as required in the IRB written procedures. The IRB Coordinator even stated during the inspection that this procedure is not being followed.

Your response dated June 8, 2004 indicated that you plan to develop policies and procedures to specifically address these deficiencies. In your written response to this letter, please provide your time frame for completion of these procedures. In addition, once the procedures have been adopted, we request that you provide copies of the procedures.

2. Failure to assure that documentation of and information given to the subjects as part of the informed consent is in accordance with 21 CFR 56.109(b)-(c) and 56.111(a)(4)-(5).

In order to approve a study, the IRB must determine that informed consent will be sought from each subject in accordance with 21 CFR Part 50. The IRB must require that information provided to subjects as part of informed

consent contains the basic elements described in 21 CFR 50.25, and that this information is documented as described in 21 CFR 50.27.

You failed to adhere to these regulations. Examples of the required elements that were missing from some informed consent documents include:

- statement that the study involves research
- the potential benefits to the subject or others
- any possible alternative procedures or courses of treatment
- a contact to call for questions about the study
- the possibility that FDA may inspect the subject's records

Of the informed consent forms we reviewed, each of these elements were missing from some of the forms approved by your IRB. Without the inclusion of such information, the study subject will not be able to make an informed decision regarding study participation.

Your June 8 response indicated that you will revise your policies and procedures to specifically address these deficiencies. In your written response to this letter, please provide your time frame for revision of these procedures. In addition, once the revised procedures have been adopted, we request that you provide copies of the procedures. Your response also referenced the development of an informed consent checklist, but did not specifically identify the purpose of the checklist. If the purpose of the checklist is to ensure the inclusion of all basic and additional elements of informed consent, as appropriate, please provide a copy of the checklist when completed.

3. Failure to conduct adequate continuing review (21 CFR 56.109)

Pursuant to 21 CFR 56.109(f), the IRB must conduct continuing review, at least once a year, of studies that it has approved.

You failed to adhere to this regulation. An example of your failure to satisfy this requirement includes but is not limited to the following:

There was no documentation that the Henrico Doctors' Hospital IRB performed continuing review for the "Emergency/Compassionate Use of the [REDACTED]™ [REDACTED] [REDACTED] [REDACTED] [REDACTED] in Patients with Aortic or Iliac Aneurysms" research study.

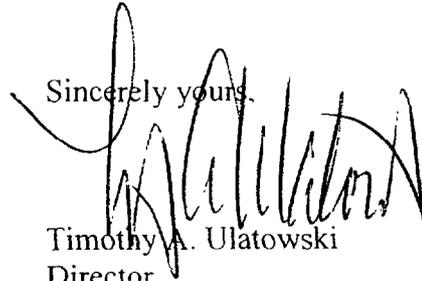
Your June 8 response regarding this deficiency appears adequate if implemented as stated. Once the revised procedures for continuing review are completed, please provide copies of the revised procedures.

4. Failure to maintain adequate documentation of IRB activities [21 CFR 56.115]

response to: Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement 1, HFZ 311, 2094 Gaither Road, Rockville, Maryland 20850. Attention: Ms. Marian J. Serge, R.N.

We are also sending a copy of this letter to FDA's Baltimore District Office, and request that you also send a copy of your response to that office. If you have any questions, please contact Ms. Serge by phone at (301) 594-4723, ext. 139, or by email at mjl@cdrh.fda.gov.

Sincerely yours,



Timothy A. Ulatowski
Director
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cc: Michael J. Decker, MD
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