HENRICO DOCTORS' HOSPITAL

September 13, 2004

Marian J. Serge RN
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, MD 20850

RE: Henrico Doctors' Hospital, Institutional Review Board
Response to FDA Warning Letter Dated August 25, 2004

Dear Ms. Serge,

This letter is in response to the Food and Drug Administration's Warning Letter to Henrico Doctors' Hospital, dated August 25, 2004.

Per the request of the Warning Letter, the following attachments are included with this correspondence, for your review:

-A copy of Henrico Doctors' Hospital Institutional Review Board's recently adopted Policies and Procedures
-A copy of Henrico Doctors' Hospital Institutional Review Board's Informed Consent Form Checklist

The Informed Consent Form Checklist is a tool to be used by sites and by the IRB Members, to ensure inclusion of all basic and additional elements of informed consent.

Forest Campus - Administration
1602 Skipwith Road
Richmond, Virginia 23229
Telephone 804 289 4800
Fax: 804 289 4801
www.HenricoDoctorsHospital.com

Additionally, we would like to provide an update on the corrective actions we proposed in our letter dated June 8, 2004.

Our experienced local consultants, Lisa Shawler, Paige Beck and Mary Crossland continue to play an active role in the implementation of our corrective actions. Consultants are present at each meeting, providing guidance and education, as well as oversight of minute recording, correspondence, and record keeping. They are committed to serving as consultants to the Henrico Doctors' Hospital Institutional Review Board and are working with Administration to develop a long term plan for the management of the IRB. As indicated in our June 8, 2004 correspondence, Henrico Doctors' Hospital has been and will continue to dedicate all necessary support and resources to correct the objectionable findings and will provide a long term commitment to the protection of human research subjects.

On June 9, 2004, correspondence was sent to all Clinical Investigators with Open Enrollment Studies, informing them of the FDA Inspection and suspending enrollment in the studies. Copies of these letters were sent to FDA and the Office of Human Research Protections as indicated. Included with these letters was a Status Report Form, which the IRB required that the sites complete and submit by July 15, 2004. These forms were also sent to Clinical Investigators with Open Studies where enrollment had been previously closed but subjects were still being followed. Completion of the form provides the IRB with information on recruitment, informed consent, screening, enrollment, study status, adverse events, and risk/benefits for each study. Additionally, the sites were required to submit new copies of study protocols, consent forms, case report forms, safety reports and Investigational Drug Brochures. The IRB has been performing substantive review of each study as the materials have been received. As part of this review, a thorough evaluation of the informed consent document has been performed and modifications are being required as indicated. Additionally, signed informed consent forms are being reviewed to further evaluate the informed consent form process. The IRB is also evaluating any activities that may have occurred during previous lapses in review. To date, substantive review has been performed or initiated on 29 studies. The remaining studies are planned for substantive review on October 1, 2004.

The IRB evaluated its Membership in comparison to types of studies reviewed. As a result, a second device specialist was added to the Committee, bringing Membership to 11 total Members, and 2 Alternates. Membership includes non-scientists, as well as an unaffiliated member.

We would also like to provide details of IRB activities since our last correspondence.

- On June 4, 2004, the Members were presented with the Inspectional Observations noted on FDA Form 483, as well as the proposed corrective actions. The local consultants presented the Members with copies of FDA Guidelines and Federal Regulations. The Members received inservices on the topics of substantive continuing review and on the informed consent process. The Members expressed support of the proposed corrective actions. No studies were reviewed at this meeting.

- The IRB met again on June 18, 2004. All Members were provided with copies of the manual entitled Protecting Study Volunteers in Research, by Cynthia McGuire Dunn MD and Gary L. Chadwick Pharm.D. MPH, CIP, Third Edition, 2004. At this meeting, Revised Policies and Procedures were presented to the IRB. Additional education was provided to the Members, through review of these Policies and Procedures. Particular emphasis was placed on the role of the IRB, device review, significant risk determination, review of advertisements, informed consent process, substantive continuing review, and record keeping. The Policies and Procedures were adopted, with modifications, at this meeting. The Committee recognizes the importance of continuous review of Policies and Procedures, and, accordingly, the Committee will modify and enhance them as indicated. No studies were reviewed at this meeting. However any newly submitted safety information was reviewed by the Committee.

- The IRB then met on July 2, 2004, July 16, 2004 and August 6, 2004. At these meetings the IRB began substantive review of studies based on the Status Report Forms received from the Investigative Sites. The IRB did not place any new protocols on these meeting agendas, as the priority of the Committee was to ensure protection of those subjects already enrolled at the Henrico Doctors' Hospital site. All Members received a packet containing materials for review one week prior to these meetings. The Primary Review process has been eliminated. Throughout these substantive reviews, the local consultants have worked with the Investigative Sites to provide education and guidance related to the IRB's Policies and Procedures, Federal Regulations, and the protection of human subjects. Findings, Requests for Modifications and Requests for Additional Information are being communicated to the Clinical Investigators in writing.

- The IRB met on September 10, 2004. At this meeting, the IRB continued with the meeting practices and substantive reviews as described above. This meeting also included the review of five new study protocols, utilizing our Revised Policies and Procedures as guidance. Additionally, the IRB reviewed and approved, with modifications, a new IRB application.

The IRB recognizes the importance of Continuing Education of its Members and Investigative Staff. Inservices will be a regular part of the IRB meeting agenda. Additionally, when appropriate, copies of educational materials will be forwarded to the Clinical Investigators. Henrico Doctors' Hospital supports continuing education of the IRB staff and is committed to ensuring that the IRB Coordinator is provided the resources to attend national educational opportunities. The IRB Coordinator will then convey this information to the IRB.

On July 22, 2004, the local consultants hosted a Lunch and Learn Inservice on the Informed Consent Process. Henrico Doctors' Hospital Investigative Sites were invited to attend the inservice. Twelve Study Coordinators with projects open at Henrico Doctors' Hospital attended this session. The feedback from the Study Coordinators was positive. The local consultants plan to conduct additional inservices to this target audience in the future. Handouts from this presentation were provided to the IRB Members in the form of an inservice at the September 10, 2004 meeting of the IRB.

As we move forward with our corrective actions, the Henrico Doctors' Hospital IRB has the following plans:

-Continuation of substantive review of all open studies
-Continuation of emphasis on the informed consent process
-Continuation of education of IRB Members and Investigative Sites
-Continuation of appropriate record-keeping processes to ensure compliance and to prevent lapse in continuing review
-Review of previously closed studies by local consultants to ensure proper closure, September 2004
-Development of a long term plan for the management of the IRB, September 2004

We look forward to working with you, as you review our corrective action update, revised Policies and Procedures and Informed Consent Form Checklist. Additionally, we are committed to taking any additional corrective action steps necessary to further our commitment to protecting human research subjects.

If we can provide further information related to our current progress and future direction, please do not hesitate to contact any of our team members through Lisa Shawler, Local Consultant, at (804) 254-5440.

Sincerely,

Patrick Farrell
CEO

Elizabeth L. Matish
Associate Administrator, IRB

Lisa G. Shawler, RN, CCRC, CIM
Local Consultant, IRB

Paige E. Beck, BA
Local Consultant, IRB

Mary C. Crossland, RN, CWCN
Local Consultant, IRB