DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 301-435-0668
FAX: 301-402-2071
E-mail: pmcneilly@osophs.dhhs.gov

September 5, 2003

Thomas A. Selden
President and Chief Executive Officer

Patricia A. Moore
Vice President, Clinical Services
Parma Community General Hospital
7007 Powers Boulevard
Parma, OH 44129-5495

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 00001661

Research Activity: **Percutaneous Transluminal Carotid Stent Placement**
Principal Investigator: **Gerald Burma, M.D.**

Dear Mr. Selden and Ms. Moore:

The Office for Human Research Protections (OHRP) has reviewed the Parma Community General Hospital's (PCGH) October 28, 2002 report in response to OHRP's letter of June 20, 2002 regarding the above-referenced research.

Based upon its review of materials submitted by PCGH, OHRP makes the following determinations:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(b)(5) require prompt reporting of unanticipated problem involving risks to subjects or others to the institutional review board (IRB), appropriate institutional officials, and the Department or Agency head. The PCGH October 28, 2002 report stated the following:

(a) "The Quality Department at PCGH reviewed all of the patients enrolled in the Study, to identify those patients who had experienced any type of complication or issue, and also identified which of such patients were the subjects of adverse event reporting forms submitted by the Principal Investigator. From that group,

the IRB identified at least three patients who it believed may have experienced complications that potentially should have been reported to the IRB, but were not reported."

(b) "..., [PCGH consulting physician] believed that three late events in the subject patient group were expected, but should nonetheless have been reported as secondary events. In addition, [PCGH consulting physician] believed that two unreported bleeding complications should have been reported as secondary/minor events, and further that these types of bleeding complications should have been included in the Study as potential adverse events (PCGH's IRB notes that hemorrhage was listed as a risk in the informed consent forms)"

(c) "... PCGH has determined that while the most serious adverse events were reported, less serious adverse events which should have been reported by the Principal Investigator were not properly reported."

OHRP finds that the principal investigator for the above-referenced research failed to report to the PCGH IRB certain unanticipated problems involving risks to subjects or others as required by HHS regulations at 45 CFR 46.103(b)(5).

Corrective Action: OHRP acknowledges that PCGH has developed corrective actions to address the above determination which includes the following:

(a) Development of a new policy for reporting adverse events. This new policy requires the retention of the reporting form by the PCGH IRB, as well as an initial review of the form pursuant to guidelines established by the PCGH IRB.

(b) Requiring the PCGH Quality Department to examine the medical records of each adverse event reported to determine if a particular patient is participating in a research study.

(c) All principal investigators will be required to document training on the conduct of clinical investigations.

OHRP finds that these corrective actions adequately address the above determination and are appropriate under the PCGH FWA.

(2) HHS regulations at 45 CFR 46.116(a)(2) require that informed consent include a description of any reasonably foreseeable risks to the subject. OHRP notes that bleeding complications, as noted in Item (1)(b) above, resulted in a gastrointestinal bleed and a large groin hematoma which were not described in the informed consent document for the above-referenced research. As a result, OHRP finds that the informed consent document for the above-referenced research failed to meet the requirements of 45 CFR 46.116(a)(2).

Required Action 1: PCGH must provide OHRP with an appropriate corrective action plan to address the above finding.

(3) OHRP finds that PCGH does not have written IRB procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(b)(4) and (5):

(a) The procedures which the IRB will follow for conducting its initial review of research.

(b) The procedures which the IRB will follow for determining which projects require review more often than annually.

(c) The procedures which the IRB will follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

(d) The procedures which the IRB will follow for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

Required Action 2: PCGH must submit to OHRP revised procedures which address the deficiencies noted in the above finding. In order to assist PCGH in revising its IRB procedures, please see OHRP guidance located on our website at http://ohrp.osophs.dhhs.gov/humansubjects/guidance/irbgd702.htm.

(4) In its June 20, 2002 letter, OHRP presented an allegation that the investigator for the above-referenced research performed right vertebral artery angioplasty and stent placement, as well as placement of an external carotid artery stent in patients and that these procedures are considered investigational. OHRP finds that the patient who underwent right vertebral angioplasty and stenting was not enrolled in the above-referenced research. In addition, OHRP finds that the placement of an exterior carotid artery stent in a subject enrolled in the above-referenced research was due to operator error in deploying the stent and was promptly reported to the PCGH IRB.

[Redacted]

Please forward your report and corrective actions so that OHRP receives it no later than October 24, 2003.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Dale H. Cowan, IRB Chair, PCGH
Ms. Darlene P. Vrotsos, IRB Administrator, PCGH
Dr. Gerald Burma, PCGH
Commissioner, FDA
Dr. David Lepay, FDA
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Yvonne Higgins, OHRP
Ms. Shirley Hicks, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Melinda Hill, OHRP