DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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December 2, 2004

Tomiko Takeda, M.Ed.
Executive Director
Colorado Cancer Research Program, Inc.
2253 South Oneida Street, Suite B
Denver, CO 80224

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 4271

Research Project: A Randomized Trial Comparing the Safety and Efficacy of Adriamycin and Cyclophosphamide Followed by Taxol to That of Adriamycin and Cyclophosphamide Followed by Taxol Plus Herceptin in Node-Positive Breast Cancer Patients Who Have Tumors That Overexpress HER2.
Principal Investigator: Eduardo R. Pajon, M.D.
Project Number: NSABP Study B-31

Dear Ms. Takeda:

The Office for Human Research Protections (OHRP) has reviewed your August 8, 2003 and October 21, 2004 reports evaluating allegations of noncompliance by the Colorado Cancer Research Program, Inc. (CCRP) with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46) involving the above-referenced research. The allegations involve the possible failure of informed consent documents for this research to include an adequate description of any additional costs to subjects pertaining to required heart monitoring scans (MUGA scans) that may result from participation in the research, as required by HHS regulations at 45 CFR 46.116(b)(3).

Based upon its review, OHRP makes the following determination regarding the protection of human subjects in this research:

(1) OHRP finds that informed consent documents approved by the IRB for the above research should have included more accurate and specific information about additional costs to subjects that could result from participation in the research, in accordance with HHS regulations at 45 CFR 46.116(b)(3). Specifically, OHRP finds that the original informed consent documents for the above-referenced study approved by the IRB on June 21, 2000, and the amended consent documents approved by the IRB on July 19, 2000, April 16, 2003, and May 2, 2003, failed to inform subjects that they or their insurers could

be billed for potentially uncovered charges for MUGA scans required by the research.

Corrective Action: OHRP finds that CCRP has taken the following corrective actions which adequately address the above finding: CCRP amended the discussion of costs in the informed consent document approved June 10, 2003 to clarify that (a) post-baseline MUGA scans required by the study would be reimbursed up to $420, (b) charges above $420 would be billed to subjects or to subjects' insurers, (c) insurers might not cover these additional charges, and (d) subjects were entitled to receive an estimate of the costs associated with the study prior to enrollment. CCRP additionally notified all MUGA scan providers who performed subjects' MUGA scans of protocol billing requirements, and informed them not to bill third-party payors for post-baseline MUGA scans. On June 10, 2003, CCRP voluntarily suspended enrollment of new subjects in the above protocol until MUGA scan billing issues could be resolved. CCRP conducted an audit of MUGA scan payments made by or on behalf of all subjects enrolled prior to the suspension. CCRP determined that 10 subjects had paid a co-payment for MUGA scans, and therefore CCRP reimbursed these subjects.

OHRP finds that the above corrective action adequately addresses the findings set forth in paragraph (1). As a result, there should be no need for further OHRP involvement in this matter.

OHRP makes the following recommendation regarding CCRP's system for human subject protections:

(2) Written IRB policies and procedures should provide a step-by-step description with key operational details for each of the procedures required by HHS regulations at 45 CFR 46.103(b)(4) and (5). Please see OHRP's Guidance on Written IRB Procedures at http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd702.htm.

OHRP appreciates CCRP's continued commitment to the protection of human research subjects. Please feel free to contact me if you have any questions.

Sincerely,

Carol J. Weil, J.D.
Compliance Oversight Coordinator
Office for Human Research Protections

cc: Dr. Sami V. Diab, IRB Chair, HealthOne Alliance IRB
Dr. Eduardo R. Pajon, CCRP
Dr. Michaele Christian, Associate Director, CTEP
Dr. Edward Romond, NSABP
Commissioner, FDA
Dr. David Lepay, FDA
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP

Dr. Michael Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Shirley Hicks, OHRP
Ms. Pat El-Hinnawy, OHRP
Ms. Janet Fant, OHRP