DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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August 20, 2004

Eugene Trani, Ph.D.
President
Virginia Commonwealth University
910 West Franklin Street
Richmond, VA 23298-0568

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 5287

Project Title: **Biomarkers of Smoke Intake, Blood Nicotine, and Urinary TSNA in Healthy Subjects Smoking Advance®-A Cigarette Produced from Tobacco Containing Low Levels of Tobacco-Specific Nitrosamines, and Equipped With Active Charcoal Filter**

Principal Investigator: **William H. Barr, Pharm.D., Ph.D.**

Dear Dr. Trani:

The Office for Human Research Protections (OHRP) has reviewed the Virginia Commonwealth University's (VCU) October 3, 2003 report, which was submitted in response to OHRP's August 26, 2003 letter.

Based upon its review of VCU's October 3, 2003 report, OHRP makes the following determinations:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(b)(4)(iii) stipulate that changes in research, during the period for which the institutional review board (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. OHRP finds that the investigator performed additional carbon monoxide testing not described in the IRB-approved protocol on one subject enrolled in the above-referenced research, prior to obtaining IRB review and approval for this additional testing.

(2) HHS regulations at 45 CFR 46.117(a) require that informed consent be documented by the use of a written consent form approved by the IRB and signed by the subject, or the subject's legally authorized representative, unless the IRB waives this requirement. OHRP finds that informed consent for additional carbon monoxide testing was not documented by a written consent form for one subject enrolled in the above-referenced research.

Required Action: VCU must provide a satisfactory corrective action plan to address the above findings. Please forward your corrective action plan so that OHRP receives it no later than October 1, 2004.

(3) It was alleged that the investigator failed to ensure that risks to subjects were minimized by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, as required by HHS regulations at 45 CFR 46.111(a)(1). In specific, it was alleged that the investigator (a) failed to have adequate medical personnel present during the course of the research, and (b) failed to obtain a medical consultation for a subject who experienced an adverse event as a result of participating in the research. Based on the materials provided in your report, OHRP finds that the above allegations could not be substantiated.

(4) It was alleged that the investigator failed to obtain the legally effective informed consent of the subject or the subject's legally authorized representative, as required by HHS regulations at 45 CFR 46.116. In specific, it is alleged that the investigator performed research testing on three subjects without obtaining their legally effective informed consent. Based on the materials provided in your reports, OHRP finds that the above allegation could not be substantiated.

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: Ms. Rosemary Kelso, HPA, VCU
Ms. Monika Markowitz, VCU
Dr. William Barr, VCU
Dr. William E. Smith, Chair, IRB #2, VCU
Dr. Ann Nichols-Casebolt, Chair, IRB # 3, VCU
Dr. Andrea Hastillo, Chair, IRB # 4, VCU
Dr. Lee Ann Hansen, Chair, IRB #5, VCU

Dr. Ronald Gadde, IRB Chair, WIRB
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Dr. Bernard Schwetz, OHRP
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Ms. Shirley Hicks, OHRP
Ms. Janice Walden, OHRP
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