DEPARTMENT OF HEALTH & HUMAN SERVICES

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September 22, 2000

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RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1315
Second Quarterly Progress Report

Dear Dr. Trani and Dr. Pickens:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed the following documents provided by Virginia Commonwealth University (VCU):

(1) VCU's second quarterly progress report dated July 31, 2000, on institutional protections for human subjects at VCU.

(2) The revised VCU Institutional Review Board (IRB) Written Policies and Procedures dated August 29, 2000.

(3) Dr. Pickens' September 13, 2000 follow-up letter and the Western Institutional Review Board's September 11, 2000 letter.

OHRP acknowledges that VCU continues to make significant progress in enhancing its system for protecting human subjects. In particular, OHRP notes that the minutes for the June 29 and

July 13, 2000 IRB-02 meetings clearly documented high-quality, detailed, and substantive reviews of research protocols that reflected the IRB's understanding of important ethical issues and regulatory requirements related to the protection of human subjects.

Additional OHRP Feedback and Guidance

(1) Regarding the VCU IRB Written Policies and Procedures, Section VI.F, **Research Involving Prisoners**, please note that for research proposing the involvement of prisoners as subjects that is supported by the Department of Health and Human Services (HHS), HHS regulations at 45 CFR 46.305(c) and 46.306(a)(1) require that institutions certify to the Secretary of HHS (i.e., to OHRP) that the IRB has fulfilled its duties under 45 CFR 46.305(a). Please see the enclosed May 19, 2000 OPRR memorandum for additional guidance on approving research involving prisoners as subjects.

(2) Regarding the July 27, 2000 version of VCU protocol #9908-4F, entitled "The Mid-Atlantic Twin Registry" (Principal Investigator: Linda Corey, Ph.D.) that was submitted to the Western IRB for review, OHRP notes the investigators' request for a waiver of informed consent for initial recruitment and enrollment of subjects in the Mid-Atlantic Twin Registry (MATR). OHRP has the following concerns regarding this request:

(a) It appears that the investigators may be confusing the requirements for IRB approval of an alteration or waiver of some or all of the requirements for obtaining informed consent [see 45 CFR 46.116(d)] with the requirements for IRB approval of a waiver of the requirement for the investigator to obtain a signed consent form from some or all of the subjects [see 45 CFR 46.117(c)].

(b) If the investigators indeed are requesting that the IRB approve a waiver of the requirement to obtain informed consent, OHRP is concerned that the justification proposed by the investigators for finding that the research could not practicably be carried out without the waiver [see 45 CFR 46.116(d)(3)] is not ethically justifiable. In specific, claiming that subject enrollment is too low when informed consent is solicited with a procedure that includes all required elements of informed consent stipulated by HHS regulations at 45 CFR 46.116 would not be an acceptable justification for the waiver.

Please include a response to these concerns with your next quarterly progress report (see below).

(3) Regarding the protocols determined to be exempt by VCU under HHS regulations at 45 CFR 46.101(b) between May 1 and June 30, 2000, it appears that the following protocols were inappropriately determined to be exempt:

(a) IRB Protocol #0002-E227, Personality and HIV Treatment Adherence. This protocol was determined to be exempt under HHS regulations at 45 CFR

46.101(b)(2). OHRP finds that this project does not meet the criteria for exemption at 45 CFR 46.101(b)(2) because (i) the research survey information is temporarily recorded in a manner that human subjects can be identified, and disclosure of the subjects responses outside the research could damage the subjects' financial standing, employability, or reputation; and (ii) the research involves obtaining information from the subjects medical records and therefore involves more than just educational tests, survey procedures, interview procedures, or observations of public behavior.

(b) IRB Protocol #0002-E178, Nursing Interventions for Patients Awaiting Cardiac Transplantation. This protocol was determined to be exempt under HHS regulations at 45 CFR 46.101(b)(2). OHRP finds that this project does not meet the criteria for exemption at 45 CFR 46.101(b)(2) because the research interview information is recorded in a manner that human subjects can be identified (i.e., by videotaping), and disclosure of the subjects responses outside the research could damage the subjects' financial standing, employability, or reputation.

(c) IRB Protocol #00812, Stress, Coping and Well-Being in Arthritic Older Women. This protocol was determined to be exempt under HHS regulations at 45 CFR 46.101(b)(2). OHRP finds that this project does not meet the criteria for exemption at 45 CFR 46.101(b)(2) because the research involves having subjects wear a motionlogger on their wrists for 24 hours and therefore involves more than just educational tests, survey procedures, interview procedures, or observations of public behavior.

(d) IRB Protocol #0002-180, A Comparison Between Child-Directed and Parent-Directed Breastfeeding Pilot. This protocol was determined to be exempt under HHS regulations at 45 CFR 46.101(b)(2). OHRP finds that this project does not meet the criteria for exemption at 45 CFR 46.101(b)(2) because the research survey information is recorded in a manner that human subjects can be identified through identifiers linked to the subject, and disclosure of the subjects responses outside the research could damage the subjects' financial standing, employability, or reputation.

(e) IRB Protocol #0002-E181, Follow-Up of Prenatally Substance Exposed Children. This protocol was determined to be exempt under HHS regulations at 45 CFR 46.101(b)(3). OHRP finds that this project does not meet the criteria for exemption at 45 CFR 46.101(b)(3) because the subjects are not elected or appointed public officials or candidates for public office. Furthermore, OHRP finds that this project would not meet the criteria for exemption at 45 CFR 46.101(b)(4) because the data being collected is recorded in a manner that subjects can be identified through identifiers linked to the subject.

Required Actions

(1) VCU's next quarterly progress report is due November 1, 2000, and should include the following:

(a) An update on VCU's progress in implementing its corrective action plans and its educational programs for members of the VCU IRBs, all IRB staff, and all research investigators about the ethical principles and regulatory requirements for the protection of human subjects.

(b) A summary of progress made by the IRBs in reviewing all current Federally supported research projects at VCU involving human subjects.

(c) Copies of the minutes for all meetings of IRB-02 and IRB-03 convened since September 1, 2000, and for the two most recent meetings of IRB-01.

(d) Copies of any revised sections of the VCU IRB policies and procedures.

(e) A report on the status of the Mid-Atlantic Twin Registry project. Please provide copies of the following documents with your status report on this registry: (i) all relevant minutes of IRB meetings related to re-review of this project since your July 31, 2000 quarterly progress report; (ii) the final version of any protocols and informed consent documents approved by the IRB; and (iii) all correspondence between the investigators and the IRB since your July 31, 2000 quarterly progress report.

(2) One of VCU's IRBs must review and approve all nonexempt research protocols that were inappropriately determined to be exempt. Such research should be suspended until appropriate IRB review and approval occurs. VCU must submit with its next quarterly progress report a satisfactory corrective action to ensure that determinations about the exempt status of protocols are appropriately made. OHRP strongly recommends that VCU review all protocols that were determined to be exempt since June 30, 2000 to ensure that no other protocols were inappropriately designated as exempt.

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

Sincerely,

Michael A. Carome, M.D.
Director, Division of Compliance Oversight

Enclosure: May 19, 2000 OPRR memorandum regarding research on prisoners

cc: Dr. Angela Bowen, President, WIRB
Mr. Ron Warren, Senior Vice President, WIRB
Ms. Marian Linde, FDA
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. John Mather, Department of Veterans' Affairs
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Dr. J. Thomas Puglisi, OHRP
Dr. Jeffery Cohen, OHRP
Dr. Clifford C. Scharke, OHRP
Dr. Katherine Duncan, OHRP
Mr. George Gasparis, OHRP