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: 240-453-8132
FAX: 240-453-6909
E-mail:kborror@osophs.dhhs.gov

February 17, 2006

William S. Dalton, M.D., Ph.D.
Chief Executive Officer/Center Director
H. Lee Moffitt Cancer Center and Research Institute, Inc.
12902 Magnolia Drive
Tampa, FL 33612

RE: Human Research Subject Protections Under Federalwide Assurance FWA-1464

Research Project: Natural History of HPV Infection in Men: The HIM Study
Principal Investigator: Dr. Anna R. Giuliano
Project Number: 1R01CA098803

Dear Dr. Dalton:

The Office for Human Research Protections (OHRP) has reviewed H. Lee Moffitt Cancer Center and Research Institute, Inc.'s (H.L. Moffitt) May 12, 2005 report responding to allegations of noncompliance 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, as outlined in OHRP's April 1, 2005 letter.

Based upon its review, OHRP notes the following regarding the above-referenced research:

(1) It was alleged that the institutional review board (IRB) failed to ensure that risks to subjects were minimized by using procedures that are consistent with sound research design, and that risks were reasonable in relation to anticipated benefits, if any, to the subjects, as required by HHS regulations at 45 CFR 46.111(a)(1) and (2). In specific, it was alleged that withholding Human Papillomavirus (HPV) test results from subjects denies the subjects the ability to protect current or future partners from HPV infection. OHRP notes the following:

(a) The original IRB that reviewed the study, the University of Arizona IRB, objected to the provision of test results to subjects, stating, "it is strongly

recommended they (male study participants) not receive testing results. These tests have not been validated and as such cannot be correlated with clinical implications."

(b) After being notified of concerns about not giving test results to subjects, the University of South Florida (USF) IRB (the IRB of record for this study at H.L. Moffitt) conducted an ethics discussion and determined in a nonunanimous vote to have test results given to subjects following appropriate quality control of the research laboratory results and accompanied by counseling of the subject. The informed consent document states, "We advise you to talk to your female partner about getting a yearly pap smear no matter what your HPV test results are."

Based on the above information, OHRP finds that the allegations cannot be substantiated.

(2) It was alleged that the above-referenced study hypothesized that current condom use confers reduced risk of incident HPV infection, when other studies have concluded that condoms do not provide effective protection against HPV infection. Such allegations are not within the purview of OHRP as they do not relate to HHS regulations at 45 CFR part 46. Therefore, OHRP makes no finding on this allegation.

As a result, OHRP anticipates no further involvement in this matter.

OHRP has the following additional guidance for H.L. Moffitt and the USF IRB:

(3) OHRP notes that potential subjects in the above-referenced research may dial a phone number to find answers to questions about the research study "and verify that the participants meet the eligibility criteria." Please note that if the phone screeners are obtaining any information from callers (whether identifiable or not), the callers are human subjects, and informed consent must be obtained from them prior to soliciting information from them, unless informed consent is appropriately waived by the IRB.

(4) Although the protocol for the above-referenced research includes providing test results to subjects following appropriate quality control of the research laboratory results, the protocol still states on page 30, "Participants will receive their HPV test results at the end of the study or when they leave the study, which ever *[sic]* is earlier.... we will not be informing participants of their HPV status until the end." OHRP recommends that these statements be removed from the protocol.

(5) Pages 15-2 through 15-4 of the USF IRB Policies and Procedures include HHS regulations at 45 CFR part 46 subpart B. Please note that these regulations were revised on November 13, 2001. OHRP recommends that the USF IRB replace the old regulation with the revised regulation in the IRB Policies and Procedures.

(6) Page 15-6 of the USF IRB Policies and Procedures refers to research subjects who subsequently become incarcerated. It states, "In such cases, the investigator must notify

the IRB immediately upon learning that the subject has become a prisoner. The IRB must then review the research at its earliest opportunity and determine whether the research is suitable for the involvement of prisoners...." OHRP notes that when a previously enrolled research subject becomes a prisoner and the relevant research protocol was **not** reviewed and approved by the IRB in accordance with the requirements of HHS regulations at 45 CFR part 46, subpart C, all research interactions and interventions with, and obtaining identifiable private information about, the now-incarcerated prisoner-subject must cease until the requirements of subpart C have been satisfied with respect to the relevant protocol. OHRP has allowed one important exception. In special circumstances in which the principal investigator asserts that it is in the best interests of the subject to remain in the research study while incarcerated, the IRB chairperson may determine that the subject may continue to participate in the research until the requirements of subpart C are satisfied.

(7) Section 15 of the USF IRB Application asks, "Does the sponsor of this study require a formal plan for data and safety monitoring?" If the applicant answers "no" to this question, they are told to go to the next section. Please note that HHS regulations at 45 CFR 46.111(a)(6) require the IRB to determine that, when appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

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,

Kristina C. Borror, Ph.D.
Director
Division of Compliance Oversight

cc:
Dr. Timothy J. Yeatman, Associate Ctr. Director for Clinical Investigations, H.L. Moffitt
Dr. Barry Bercu, Chair, IRB #1, USF
Dr. Paul Stiles, Chair, IRB #2, USF
Dr. Anna R. Giuliano, H.L. Moffitt
Commissioner, FDA
Dr. David Lepay, FDA
Dr. Lana Skirboll, Director, Office of Science Policy, NIH
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Ms. Irene Stith-Coleman, OHRP
Ms. Shirley Hicks, OHRP
Ms. Janet Fant, OHRP
Ms. Patricia El-Hinnawy, OHRP