DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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October 13, 2004

John Agwunobi, M.D., M.B.A.
Secretary of Health
Florida Department of Health
4052 Bald Cypress Way, Bin A-07
Tallahassee, Florida 32399-1708

RE: Human Research Subject Protections Under Federalwide Assurance (FWA) 4682

Dear Dr. Agwunobi:

The Office for Human Research Protections (OHRP) has reviewed your September 10, 2004 report that was submitted in response to OHRP's August 31, 2004 letter to the Florida Department of Health (FDOH) regarding determinations of noncompliance with the Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 CFR part 46). These determinations were based upon OHRP's August 17-19, 2004 on-site evaluation of human subject protection. OHRP has determined that the corrective actions summarized below adequately address the findings presented in OHRP's August 31, 2004 letter and are appropriate under the FDOH's FWA.

(1) The first footnote following HHS regulations at 45 CFR 46.101(i) states that the exemptions at 45 CFR 46.101(b) do not apply to research involving prisoners (Subpart C). OHRP found that Protocol #1070, "Evaluation of HIV/AIDS Case Reporting of Prisoners in Florida," was inappropriately determined to be exempt, in contravention of Footnote 1 following 45 CFR 46.101(i).

Corrective Action: OHRP acknowledges that the FDOH IRB will review the above study under 45 CFR part 46, subpart C, at its next continuing review and send a Subpart C prisoner certification to OHRP. In addition, the FDOH IRB will review all active studies that are open for enrollment and involve vulnerable populations for compliance with applicable federal regulations, including 45 CFR part 46, subparts B, C and D. IRB members and staff will receive education specific to vulnerable populations.

(2) HHS regulations at 45 CFR 46.116(d) require that the IRB find and document four specific criteria when approving waiver or alteration of some or all of the required elements of informed consent. OHRP found that the FDOH IRB failed to document the

four required criteria for waiver of informed consent when reviewing studies #1351 and #1366.

Corrective Action: OHRP acknowledges FDOH's statement that, for all future reviews of protocols requesting waiver or alteration of some or all of the required elements of informed consent, the FDOH IRB will consider specifically the four criteria required under 45 CFR 46.116(d). Further, at each IRB meeting, IRB members will have available a copy of the IRB Policy and Procedures Manual and applicable federal regulations. The IRB's findings and justifications for approval or disapproval will be documented in the meeting minutes.

(3) HHS regulations at 45 CFR 46.305-306 require specific findings on the part of the IRB for approval of research involving prisoners. OHRP's discussions with IRB members and its review of IRB documents revealed no evidence that the FDOH IRB makes the required findings when reviewing such research.

Corrective Action: OHRP acknowledges FDOH's statement that, for all future reviews of protocols involving prisoners, whether new submissions, continuing reviews, or amendments, the FDOH IRB will specifically consider and adequately discuss the findings required by 45 CFR part 46, subpart C; and, as recommended by OHRP, the FDOH IRB will document their findings in the meeting minutes. In addition, whenever such research is supported by HHS, the IRB will send a letter to OHRP certifying that the study was reviewed pursuant to HHS regulations at 45 CFR part 46, subpart C.

(4) HHS regulations at 45 CFR 46.404-407 require specific findings on the part of the IRB for approval of research involving children. OHRP's discussions with IRB members and its review of IRB documents revealed little evidence that the FDOH IRB makes the required findings when reviewing research involving children.

Corrective Action: OHRP acknowledges that, for all future reviews of protocols involving children, whether new submissions, continuing reviews, or amendments, the FDOH IRB will specifically consider and adequately discuss the findings required by 45 CFR part 46, subpart D; and, as recommended by OHRP, the FDOH IRB will document their findings in the meeting minutes. Additionally, relevant comments made by the child representative of the IRB will be documented in the meeting minutes.

(5) OHRP found that the institution does not have written IRB procedures for ensuring prompt reporting to appropriate institutional officials, the Department or Agency head, and OHRP of any unanticipated problems involving risks to subjects or others, as required by HHS regulations at 45 CFR 46.103(a) and (b)(5).

Corrective Action: OHRP acknowledges FDOH's statement that FDOH will incorporate the reporting procedures required by 45 CFR 46.103(a) and (b)(5) in the IRB Policy and Standard Operating Procedures Manual and the Principal Investigator's Procedure Manual. In addition, principal investigators and IRB members will receive additional education regarding the procedures for prompt reporting of unanticipated problems involving risks to subjects or others.

(6) HHS regulations at 45 CFR 46.110(b)(2) permit use of expedited procedures for review of minor changes to previously approved research. For protocol #0973 involving prisoner research, the IRB approved a modification using expedited review procedures of the original study design that incorporated the use of focus groups and in-jail, audio-recorded interviews. OHRP expressed concern that the IRB appears to have employed expedited procedures to review changes that appear to be more than minor changes.

Corrective Action: OHRP acknowledges FDOH's statement that in the future, meeting minutes will document the justification for using expedited review pursuant to 45 CFR 46.110(a) and will specify the category under which the review is expedited. If a review is expedited pursuant to 45 CFR 46.110(b)(2), the minutes will note the justification for categorizing the change as minor. In addition, the FDOH IRB will keep a log of expedited reviews involving minor changes.

(7) HHS regulations at 45 CFR 46.116 state that an investigator shall seek informed consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence. OHRP expressed concern that the placement of escalating cash values related to temporal participation in the study on the first page of the consent document for Protocol #1261, " HIV Prevention in Haitian Youths," may increase the possibility of undue influence.

Corrective Action: OHRP acknowledges FDOH's plans for increased scrutiny of recruitment materials and the consent form language at the next continuing review of the above-referenced protocol, and at future initial and continuing review of all protocols.

As a result of these determinations, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified that might alter this determination.

OHRP appreciates your institution's commitment to the protection of human subjects. Please do not hesitate to call me if you have any questions.

Sincerely,

Karena Cooper, J.D., M.S.W.
Compliance Oversight Coordinator
Division of Compliance Oversight, OHRP

cc: Ms. Nancy Humbert, FDOH
Dr. Susan Philips, FDOH
Dr. Paul Arons, IRB Chair, FDOH
Ms. Lynn H. Riley, CPA, FDOH
Dr. Bernard Schwetz, OHRP
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Ms. Patricia El-Hinnawy, OHRP
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