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August 28, 2006

Daniel H. Winship
Chief
Cook County Bureau of Health Services
1900 West Polk Street
Suite 220
Chicago, IL 60612

RE: Human Research Subject Protections Under Multiple Project Assurance M-1150 and Federalwide Assurance FWA-1802

Research Project: Phase I/II Study: Ritonavir Therapy in HIV-I Infected Infants and Children

Project Number: ACTG #345

Principal Investigator: Kenneth Boyer, M.D.

Research Project: Phase I Trial: Safety and Effectiveness of Four Anti-HIV Drug Combinations in HIV-Infected Children and Teens

Project Number: ACTG #377

Principal Investigator: Kenneth Boyer, M.D.

Dear Mr. Winship:

The Office for Human Research Protections (OHRP) has reviewed the Cook County Bureau of Health Services' (CCBHS) July 27, 2006 response to OHRP's June 19, 2006 letter regarding indications of possible 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.

In its February 17, 2006 letter, OHRP made the following determination regarding the above-referenced research:

- (1) HHS regulations at 45 CFR 46.404-409 require specific findings on the part of the institutional review board (IRB) for approval of research involving children. OHRP's

review of CCBHS IRB documents for the above-referenced research revealed no evidence that the CCBHS IRB considered and made the required findings when reviewing this research involving children.

Corrective Action: CCBHS stated in its March 29, 2006 response to OHRP that it has a standing policy that indicates “...that no minor is to be enrolled in any study that is neither minimal risk nor for the potential benefit of the minor unless a justification is documented in the minutes that the study is for the potential benefit of the group as a whole.” CCBHS also stated that they had created new IRB submission forms that explicitly ask the principal investigator to address whether the proposed study meets the criteria for either HHS regulations at 45 CFR 46.404 or 45 CFR 46.405.

OHRP notes that the revised policy entitled “Cook County Bureau of Health Service IRB Human Participant Research Policy: Inclusion of Minors” includes the following statements:

A protocol <sic> then approved for the use of Minors, only if it is in compliance with the federal regulations 45CFR46 Subpart D. The protocol must specifically state that it is of minimal risk or for the potential benefit of the child.

If a protocol is not of minimal risk or for the direct benefit of the child who is the subject it may be approved for the benefit of the larger community of children. However, this protocol must be approved as a special case. The minutes must record the discussion leading to the approval for the larger community of children and the vote must indicate that approval is in compliance with 45CFR46.406.

Wards of the State and foster children may *not* [emphasis in original] be enrolled in studies approved under 45CFR46.406.

OHRP acknowledges that Section D-III.c of the CCBHS IRB protocol submission form, entitled “Research Project Summary,” asks the investigator to indicate whether a study involving minors should be approved under either 45 CFR 46.404, 46.405 or 46.406.

In its June 19, 2006 letter, OHRP made the following additional determinations:

(2) OHRP found that when reviewing the above-referenced research, the CCBHS IRB failed to obtain sufficient information to make the following determinations required for approval of research under HHS regulations at 45 CFR 46.111:

(a) 45 CFR 46.111(a)(3). OHRP found that CCBHS IRB records for the above-referenced research demonstrated a failure of the IRB to obtain sufficient information regarding the selection of wards of the state and foster children as research subjects in contravention of

OHRP asked CCBHS to include in their corrective action a description of the manner in which the CCBHS IRB ensures that it receives sufficient information to make the determinations at 45 CFR 46.111(a)(3) for all research that it reviews.

Corrective Action: OHRP notes that the policy entitled “Cook County Bureau of Health Services IRB Human Participant Research Policy: Inclusion of Wards of the State and Foster Children in Human Subject Research,” includes the following statements:

1. If a protocol is to include Wards of the State or foster children, it must state this is the case in the IRB protocol submission and have specific IRB approval to do so prior to the inclusion of such minors.
4. The protocol submission must include an answer to each question regarding the inclusion of minors.
7. A protocol revision which amends a protocol to potential <sic> include wards of the state of <sic> foster children must be reviewed by the full board at a convened meeting. The minutes shall reflect the deliberations of the Board regarding all equitable selection <sic> and appropriate documentation.

OHRP notes that section D.IV of the CCBHS IRB protocol submission form includes the following question: “Please indicate how Wards of the state and foster children are recruited into this study.”

(b) 45 CFR 46.111(a)(4). OHRP found that CCBHS IRB records for the above-referenced research demonstrated a failure of the IRB to obtain sufficient information regarding the process for obtaining permission of parents or guardians for wards of the state or foster children.

OHRP asked that CCBHS to describe in its corrective action the manner in which the CCBHS IRB ensures that it receives sufficient information to make the determinations at 45 CFR 46.111(a)(4) for all research that it reviews.

Corrective Action: The corrective action plan submitted by CCBHS consists of the same policy referenced in item 2(a) above. OHRP notes that this policy includes the following statement: “(6) IRB minutes will reflect the justification of <sic> the inclusion of Wards or <sic> the State or foster children and the method by which permission is to be obtained from the parents or guardians.”

OHRP notes that Section IV of the CCBHS IRB protocol application includes the following question: “Who will consent for these children? If non-guardian

parents, grandparents or other relatives are available, please describe their role in the consent procedure.”

(c) 45 CFR 46.111(b). OHRP found that CCBHS IRB records for the above-referenced research demonstrated a failure of the IRB to obtain sufficient information regarding additional safeguards with respect to the enrollment of wards of the state or foster children where some or all of the subjects are likely to be vulnerable to coercion or undue influence.

OHRP asked CCBHS to describe in their corrective action plan the manner in which the CCBHS IRB ensures that it receives sufficient information to make the determinations at 45 CFR 46.111(b) for all research that it reviews.

Corrective Action: OHRP notes that the policy entitled “Cook County Bureau of Health Services IRB Human Participant Research Policy: Consent of Vulnerable Subjects including Wards of the State and Foster Children in Human Subject Research,” includes the following statements:

1. The potential inclusion of vulnerable subjects must be indicated on the IRB protocol submission form.
7. The investigator will be asked and the IRB will review any possible reasons that the vulnerable subject may be coerced to consent to the research.

OHRP notes that section D.III.c of the CCBHS IRB protocol submission form includes the following question: “What steps are taken to avoid coercion of vulnerable subjects.” Section D.IV contains a question as follows: “Additional Protection of Wards of the State and Foster Children.”

OHRP has determined that the corrective actions above adequately address OHRP’s findings. As a result, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

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,

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

cc: Lynda Brodsky, Director, Research Affairs, Cook County Bureau of Health Services
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