DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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August 26, 2004

Roberta Luskin-Hawk, M.D.
President
AIDS Research Alliance-Chicago
2800 North Sheridan Road, Suite 108
Chicago, Illinois 60657

Ronald E. Struxness, M.H.A.
Executive Vice President and CEO
Saint Joseph Hospital
2900 North Lake Shore Drive
Chicago, Illinois 60657

RE: Human Research Subject Protections Under Federalwide Assurances (FWA) 4282 and 2823

Research Project:	A Randomized, Open-Label Study of the Impact of Two Doses of Subcutaneous Recombinant IL-2 (Proleukin) on Viral Burden and CD4+ Cell Count in Patients with HIV-1 Infection and CD4+ Cell Counts $\geq$ 300/mm^3
Principal Investigator:	Roberta Luskin-Hawk, M.D.
Project Number:	CPCRA 059
HHS Award Number:	2U01 AI42199-09

Dear Dr. Luskin-Hawk and Mr. Struxness:

The Office for Human Research Protections (OHRP) has reviewed the AIDS Research Alliance-Chicago's (ARAC) May 26, 2004 report and Catholic Health Partners' (CHP) July 2, 2004 report, which were submitted in response to OHRP's April 5, 2004 letter regarding allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 CFR part 46) involving the above-referenced research.

OHRP has also reviewed the additional documentation requested by OHRP regarding the Saint Joseph Hospital (SJH) Institutional Review Board (IRB), submitted by ARAC on July 28, 2004.

OHRP has determined that the corrective actions summarized below appropriately address the findings in items (1), (3), (11), and (13) and the concern in item (14) as described in OHRP's letter of April 5, 2004 and are appropriate under the ARAC Assurance.

(1) OHRP acknowledges that the CHP IRB transferred oversight of all human subject research conducted at SJH to the SJH IRB effective July 30, 2002.

(2) OHRP acknowledges CHP's October 14, 2003 response to the Food and Drug Administration's (FDA) April 11, 2003 letter stating that the CHP IRB will be disbanded because human subject research is not currently being conducted at St. Anthony Hospital (SAH).

(3) ARAC now requires that all new research protocols be submitted to the SJH IRB with the pertinent Investigator Brochures (IB), and each updated IB is submitted to the SJH IRB within two months of its receipt by ARAC.

(4) OHRP acknowledges that according to SJH IRB policy, the IRB does not accept proxy votes and does not conduct IRB meetings in the absence of a quorum or a community representative.

(5) Dr. Luskin-Hawk has resigned her membership from the SJH IRB.

Based on its evaluation of the above-referenced ARAC report and documentation regarding the SJH IRB, OHRP makes the following determinations about the SJH IRB:

(6) HHS regulations at 45 CFR 46.107(a) require that the IRB have members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB shall be sufficiently qualified through the experience and expertise of its members to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. OHRP finds that the SJH IRB minutes for November 3, 2003 record the informal designation of an alternate for a regular voting member. OHRP notes that an alternate member(s) may be designated, as needed, for regular voting member(s). However, these alternates should be formally appointed and identified on the IRB roster. The appointment of an alternate member(s) should be based on expertise corresponding to that of the regular voting member(s).

(7) HHS regulations at 45 CFR 46.109(e) require that continuing review of research be conducted by the IRB at intervals appropriate to the degree of risk and not less than once per year. The regulations make no provision for any grace period extending the conduct of the research beyond the expiration date of IRB approval. OHRP finds that the SJH IRB minutes for June 4, 2003 and December 3, 2003 record instances in which the IRB failed to conduct continuing review of research at least once per year.

The IRB and investigators must plan ahead to meet required continuing review dates. If an investigator has failed to provide continuing review information to the IRB, or if the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research must stop, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval.

(8) HHS regulations at 45 CFR 46.115(a)(2) require that minutes of IRB meetings be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions, including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. OHRP finds that SJH IRB minutes often failed to meet these requirements.

Action 1 - Required: By October 8, 2004, SJH must submit to OHRP a detailed corrective-action plan to address the findings (6)-(8).

(9) OHRP finds that SJH does not have written procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5):

(a) The procedures which the IRB will follow for conducting its initial review of research.

(b) The procedures which the IRB will follow for conducting its continuing review of research.

(c) The procedures which the IRB will follow for determining which projects require review more often than annually.

(d) The procedures which the IRB will follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

(e) The procedures which the IRB will follow for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which 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.

(f) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, any Department or Agency head, and OHRP of: (i) any unanticipated problems involving risks to subjects or others; (ii) any serious or continuing noncompliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and (iii) any suspension or termination of IRB approval.

Action 2 - Required: By October 8, 2004, SJH must submit to OHRP revised written IRB policies and procedures that adequately describe the operational details of all activities stipulated by HHS regulations at 45 CFR 46.103(b)(4) and (5). In order to assist SJH in this matter, please refer to the enclosed "Guidance on Written IRB Procedures."

OHRP has the following supplemental guidance:

(10) OHRP strongly recommends that institutions develop and distribute a handbook of IRB guidelines for research investigators. The handbook should include detailed information concerning (a) federal and institutional requirements for the protection of human research subjects; (b) the IRB's role and responsibilities; (c) the requirements and procedures for initial and continuing IRB review and approval of research; (d) the rationale and procedures for proposing that the research may meet the criteria for expedited review; (e) the requirements and procedures for verifying that research is exempt from IRB review; (f) the responsibilities of investigators during the review and conduct of research; (g) the requirements and procedures for notifying the IRB of unanticipated problems or events involving risks to subjects, as well as any other expected or unexpected adverse events; (h) an explanation of the distinction between FDA requirements for the emergency use of test articles and HHS regulations for the conduct of human subjects research; (i) relevant examples and user-friendly forms for providing information to the IRB; and (j) a copy of

the institution's FWA, the HHS human subjects regulations (45 CFR part 46), and *The Belmont Report*. Where appropriate, OHRP also recommends that IRBs develop written operating procedures to supplement their guidelines for investigators.

Please provide your responses to the above findings to OHRP no later than October 8, 2004.

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,

Robert J. Meyer
Compliance Oversight Coordinator
Division of Compliance Oversight

Enclosure - Guidance document

cc with enclosure:
Dr. David M. Berkson, IRB Chairperson, SJH

cc without enclosure:
Mr. Edward M. Goodwin, ARAC
Ms. Kathleen K. DeVine, CHP
Mr. Mathias D. Maguire, CHP
Ms. Aileen Brooks, SAH
Commissioner, FDA
Dr. David A. Lepay, FDA
Dr. Bernard A. Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael A. Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Shirley Hicks, OHRP
Ms. Janice Walden, OHRP
Ms. Melinda Hill, OHRP
Ms. Patricia El-Hinnawy, OHRP