DEPARTMENT OF HEALTH & HUMAN SERVICES

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William A. Yost, Ph.D.
Acting Vice President for Research
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6525 North Sheridan Road
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RE: Human Research Subject Protections Under Single Project Assurance (SPA) S-5858 and Federalwide Assurance (FWA) 00000104

Dear Dr. Yost:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed Loyola University Chicago's (LUC's) report of June 29, 2000 that was submitted in response to OPRR's May 10, 2000 letter to LUC regarding allegations of possible noncompliance with the Department of Health and Human Services (HHS) regulations for protection of human subjects (45 CFR Part 46). OHRP has also reviewed LUC's letter of July 15, 2002 with attached documentation submitted in response to OHRP's July 9, 2002 request for LUC's current written institutional review board (IRB) policies and procedures.

Based upon its review, OHRP makes the following determinations:

(1) 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. OHRP expressed concern that the LUC IRB may have failed to conduct meaningful continuing review of research at least once a year.

LUC's report stated the following in response:

> "Based on the responses to the Application for Renewal, The (sic) Chair of the IRB either approves the continuation and sends the Continuing Approval Letter to the investigator or communicates, in writing, to the investigator about the submission of an amended or new IRB application. These actions are reported at the appropriate IRB meeting.
>
> My investigation revealed that these procedures were followed for most of the projects reviewed by the IRB over the past three years. However, for a few research projects, LU was unable to locate a record of continuing review. This was due either to: 1) an investigator's failure to return the Continuing Review Form; 2) the IRB files not accurately reflecting actions taken by the IRB and the investigators in relationship to applying for and obtaining approval for continuing research; or 3) the actions taken by the Chair of the IRB or by the Compliance Officer of the Office of the Associate Vice President for Research not being recorded in the IRB minutes."

Based on LUC's statements above and review of the documentation submitted with LUC's June 29, 2000 report, OHRP finds that, in certain instances, the LUC IRB failed to conduct continuing review of ongoing research at least once per year as required by HHS regulations at 45 CFR 46.109(e). The regulations make no provision for any grace period extending the conduct of the research beyond the expiration date of IRB approval. 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 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.

(2) HHS regulations at 45 CFR 46.115(a) require that the institution prepare and maintain adequate documentation of IRB activities. In its review of the LUC IRB's records submitted with LUC's July 29, 2000 report, OHRP found numerous instances of incomplete documentation of IRB actions related to the review and approval of research.

(3) HHS regulations at 45 CFR 46.110(b)(1) limit the use of expedited review procedures for both initial and continuing review to specific research categories published in the Federal Register (FR) Notice of November 9, 1998 [63 FR 60364 - 60367] that present no more than minimal risk to human subjects. Paragraph (C) of the Applicability section of the November 9, 1998 FR Notice states the following:

> "The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal."

OHRP notes that the LUC IRB approved a research protocol entitled "Risky Context and Exposure to Violence in Urban Youth" [IRB Protocol # 71844], which states the following:

> (a) "Students and parents are made aware that they will be answering questions about violence in many aspects of their lives, including possible violence and abuse in their homes. The consent forms also allow for discontinuation in the study, and inform participants that we are mandated by law to report any cases of suspected child abuse or neglect."
>
> (b) "Confidentiality will only be breached in cases of suspected child abuse and/or neglect. Protocols for reporting child abuse and neglect will be developed and implemented in all cases of suspected problems."

Based on the protocol statements above, the use of an expedited review procedure would be precluded for the IRB approval of Protocol # 71844 since, by law, protections cannot be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. Based on its review of the LUC IRB records, OHRP finds that the LUC IRB inappropriately conducted continuing review of Protocol # 71844 by the used of an expedited review procedure on October 21, 1999.

Corrective action: After reviewing LUC's revised written IRB polices and procedures (Procedures) submitted with its July 15, 2002 letter, OHRP finds that LUC has implemented changes to the Procedures that adequately address the above findings of noncompliance. LUC

has also implemented a program to educate IRB members, investigators and research staff on an ongoing basis about the ethical principles and regulatory requirements for the protection of human subjects. OHRP finds that these corrective actions are satisfactory and appropriate under the LUC FWA and adequately address findings (1) through (3) above.

(4) HHS regulations at 45 CFR 46.109(a) require that the IRB must review and approve all non-exempt human subject research covered by an assurance. OHRP expressed

concern that certain human subject research may have been conducted by graduate students without IRB review and approval.

LUC's report stated the following in response:

> "All research involving human subjects at LU is reviewed by the IRB. My investigation found no cases in the past three years in which research involving human subjects was conducted without IRB approval. With respect to the specific allegation about graduate student research, all graduate students receiving the Doctor of Philosophy (PhD), Master of Arts (MA), and Master of Science (MS) degrees must have their thesis and dissertation research projects approved by the Graduate School. This approval involves certification that the research had IRB approval if the use of human subjects was involved. A review of the Graduate School's records confirmed that all theses and dissertations over the past three years had proper IRB approval."

OHRP acknowledges LUC's statement. Based upon review of the submitted documentation and LUC's revised Procedures, OHRP finds that LUC has adequately responded to this concern.

(5) HHS regulations at 45 CFR 46.101(b) delineates research categories that are exempt from HHS regulations at 45 CFR 46. OHRP was concerned that LUC may have applied exempt status to human subject research activities that exceeded the categories of exempt research delineated by HHS regulations.

LUC's report stated the following in response:

> "Full IRB approval is required at LU for the application of exempt status. In addition, no funded research project may be granted exempt status. A review of the IRB records over the past three years shows that all applications of exempt status followed

the LU procedures and that exempt status was only granted when the research activities were consistent with the categories listed in 45 CFR 46.101(b)."

OHRP acknowledges LUC's statements. Based upon review of the submitted documentation and LUC's revised Procedures, OHRP finds that LUC has adequately responded to this concern.

As a result of the above 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 which might alter this determination.

At this time, OHRP would like to provide the following additional guidance:

(6) OHRP recommends that documentation for initial and continuing reviews conducted under an expedited review procedure include: (a) the specific permissible categories (see 63 FR 60364-60367 at http://ohrp.osophs.dhhs.gov/humansubjects/guidance/ expedited98.htm) justifying the expedited review; and (b) documentation of the review and action taken by the IRB chairperson or designated reviewer and any findings required under the HHS regulations.

OHRP appreciates the commitment of LUC 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

cc: Michael J. Garanzini, S.J., President, LUC
Patricia A. Rupert, Ph.D., Chair, IRB-01, LUC
Dr. John Mather, Director, Office of Research Compliance and Assurance, Veterans Health Administration

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