DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Public Health
and Science

Office for Human Research Protections
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February 27, 2006

Gunnar Svedberg
Vice Chancellor
Gothenburg University
P. O. Box 100
SE 405 30 Gothenburg, SWEDEN

RE: Human Research Subject Protections Under Federalwide Assurance FWA- 848

Dear Dr. Svedberg:

The Office for Human Research Protections (OHRP) has reviewed the Gothenburg University's (GU) November 14, 2005 and January 28, 2006 emails responding to OHRP's October 3, October 31, and November 22, 2005 letters regarding compliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46).

As outlined in OHRP's November 22, 2005 letter, the following actions are required for reinstatement of FWA-848:

(1) GU must develop a satisfactory corrective action plan to address all deficiencies and concerns described.

(2) GU must submit written institutional review board (IRB) procedures that adequately describe all activities referenced in HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5).

(3) The IRB must submit a satisfactory plan to re-review all HHS or U.S. federally-supported human subject protocols that have not had adequate continuing review.

(4) GU must provide a complete list of all U.S. federally supported research protocols that were suspended. Include the project title, principal investigator, IRB project number, and the Federal department or agency project number. GU should identify those projects

for which GU determines that research activities in previously enrolled subjects may continue because it is in the best interests of the individual subjects. Please describe the procedures used to make such determinations.

(5) GU must submit to OHRP a revised FWA for GU signed by a new Authorized Institutional Official. This official should reside at an administrative level above Dr. Iwarson.

OHRP acknowledges that GU has provided OHRP with a description of the legislation and procedures for the Regional Ethics Board, which GU plans to designate as the IRB under the GU assurance. However, OHRP notes that written procedures are not included for the following activities, which are 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 continuing review of research.

(b) The procedures which the IRB will follow for reporting its findings and actions to investigators and to the institution.

(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: (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and (c) any suspension or termination of IRB approval.

Required Action: Please provide OHRP with written IRB procedures to address these activities. (Please see OHRP's Guidance on Written IRB Procedures at http://www.hhs.gov/ohrp/humansubjects/guidance/irbgd702.htm)

OHRP acknowledges that GU has agreed to perform annual review of research at the request of the researcher.

Required Action: Please provide OHRP with copies of the minutes from the IRB meetings in which continuing review of all U.S. federally supported human subjects research has occurred, as required by Required Action #3 above.

OHRP notes GU's assertion that the Regional Ethics Board does not have the authority to stop an ongoing project or suspend research. Please note that HHS regulations at 45 CFR 46.113 state that an IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Therefore, in order to be compliant with HHS regulations, the Regional Ethics Board must have the authority to terminate its approval of HHS-supported research, or an IRB must be designated under the GU assurance which has this authority. Please respond.

OHRP acknowledges that GU has complied with Required Action #4 above and provided OHRP with the requested information about all U.S. federally supported human subjects research. OHRP acknowledges GU's statement that GU will be providing OHRP with information regarding Required Actions #1 & #5.

While OHRP acknowledges that GU is working on the other requirements for reinstatement of the FWA, until those requirements are completed to OHRP's satisfaction, the GU assurance, **FWA- 848, remains suspended.** As noted in OHRP's October 3, 2005 letter, this means that all U.S. federally supported human subjects research projects to which the FWA applies **must be suspended**. For any project affected by this suspension, enrollment of new subjects **must cease immediately** except in cases approved in advance by OHRP (OHRP would expect approval requests for such cases to be rare). Furthermore, research activities involving **previously enrolled subjects may continue only where it is in the best interests of such subjects**. For each affected protocol this suspension must remain in effect until OHRP approval of the FWA is reinstated.

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. Sten Iwarson, Professor, Department of Infectious Diseases, GU
Dr. Bo Risberg, Human Protections Administrator, GU
Dr. Anders Fasth, IRB Chair, GU Hosp / East
Dr. Lana Skirboll, OD, NIH
Commissioner, FDA
Dr. David Lepay, FDA
Dr. Bernard Schwetz, OHRP

Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Janet Fant, OHRP