DEPARTMENT OF HEALTH & HUMAN SERVICES

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RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1183

Research Project: Improved CPR via Telephone– A Randomized Trial
Principal Investigator: Alfred P. Hallstrom, Ph.D.
Protocol Number: R18 HS05280

Research Project: Computer-Aided Dispatching for Emergency Medical Services and a Randomized Trail of Two CPR Messages
Principal Investigator: Alfred P. Hallstrom, Ph.D.
Protocol Number: R01 HS06125

Research Project: Assessing the Technology of CPR Strategies: A Randomized Trial
Principal Investigator: Alfred P. Hallstrom, Ph.D.
Protocol Number: R01 HS08197

Dear Dr. Kwiram and Ms. McGough:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your report of February 12, 1999, regarding the above referenced research conducted at the University of Washington (UW). We apologize for the

delay in responding to your report.

Based upon its review, OHRP has made the following determinations regarding the above-referenced research:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.116(d) require that the Institutional Review Board (IRB) find and document four specific criteria when approving waiver or alteration of some or all of the required elements of informed consent. OHRP's review of IRB documents revealed no evidence that the IRB satisfied these requirements for waiver of informed consent for collapse victims, 911 callers, and dispatchers in the above-referenced research.

Moreover, according to documents describing the study provided to OHRP, if appears that this research involved greater than minimal risk to the subjects and therefore would not have satisfied the requirement for waiver of informed consent under 45 CFR 46.116(d)(1) for collapse victim subjects, and possibly 911 callers and dispatchers. HHS regulations at 45 CFR 46.102(i) defines minimal risk as meaning that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. In addition, for some subjects it appears that is would have been appropriate to provide additional pertinent information after participation, in accordance with HHS regulations at 45 CFR 46.116(d)(4).

(2) HHS regulations at 45 CFR 46.117(c) require specific findings on the part of the IRB for waiver of the usual requirements for the investigator to obtain a signed consent form from all subjects. OHRP's review of IRB documents revealed no evidence that the IRB made the required findings when approving such a waiver for the follow-up interviews of 911 callers.

(3) OHRP finds that the informed consent documents reviewed and approved by the IRB for this research for dispatchers and follow-up interviews of 911 callers failed to include the following elements required by HHS regulations at 45 CFR 46.116(a):

(a) Section 46.116(a)(1): An adequate explanation of the purposes of the research and a complete description of the procedures to be followed.

(i) The stated goal of the research in the informed consent document was "to help us to develop better communication procedures for emergency system dispatchers...," Whereas the goal of the research, according to "Assessing the Technology of CPR Strategies: A Randomized Trial," was to investigate the relative benefits of two forms of instruction for CPR provided by the dispatcher.

(ii) The informed consent document stated that callers would be asked questions regarding "events prior to, and during, the incident and the help offered by the fire department dispatcher during your call," whereas most of the interview questions dealt with the health of the patient and the outcome of the arrest.

(b) Section 46.116(a)(2): An adequate description of the reasonably foreseeable risks and discomforts. OHRP notes that no risks or discomforts were described.

(4) OHRP finds that the procedures for enrolling the dispatcher subjects failed to minimize the possibility of coercion or undue influence as required by HHS regulations at 45 CFR 46.116.

In particular, OHRP notes that a January 3, 1989 letter from Chief Claude Harris of the Seattle Fire Department stated that "[c]ompliance with the study's interrogation and CPR protocol has become department policy and dispatcher compliance is mandatory." Therefore, individuals could be fired for not taking part in the research. Indeed, there is evidence that dispatchers were fired for "non-compliance." A progress report for "Computer Aided Dispatching and a Trial of CPR Methods" stated that "[d]uring the current year we have continued to insure maximum adherence to the protocol by the dispatcher. The dispatch office has been very supportive of this effort, replacing several 'old line' dispatchers who were resistant to change...."

Required Action: By May 31, 2001, UW must submit to OHRP satisfactory action plans to address findings (1) - (4) above. OHRP acknowledges that the UW IRB has made some changes to address these issues, including requiring submission of a new application nine years after initial review. OHRP notes that subject accrual for this research has ended.

(5) HHS regulations at 45 CFR 46.115(a)(2) require that the minutes of IRB meetings document the vote on all IRB actions including the number of members voting for, against, and abstaining. OHRP finds that prior to 1997 minutes of the UW IRB failed to satisfy this requirement.

Corrective Action: OHRP acknowledges that the IRB now records votes by hand to reduce voting record errors. This procedure should adequately address these concerns in the future.

(6) HHS regulations at 45 CFR 46.115 (b) require that the IRB records relating to research shall be retained for at least 3 years after completion of the research. OHRP finds that the IRB failed to retain records for at least 3 years after completion of the trial.

Corrective Action: OHRP acknowledges that the IRB records will now be archived as permanent records. OHRP has determined that this corrective action adequately

addresses this finding and is appropriate under the UW Multiple Project Assurance (MPA).

OHRP has the following additional concerns and questions regarding the above-referenced research:

(7) It is not clear if this protocol involved children and infants. An ABC-CPR was developed for children and infants. Monthly enrollment sheets in a Progress report for "Computer Aided Dispatching and a Trial of CPR Methods" listed "Child." In addition the protocol for "Assessing the Technology of CPR Strategies: A Randomized Trial" stated that exclusions, such as being under the age of 18, were determined later when the telephone call was abstracted or the run report reviewed. A screening form for dispatches (to be filled out after the call when field reports were available) had a check off for "legitimate randomization" and under "yes" several exclusions were listed to be indicated, one of them being "age < 18." Please respond. In your response, please clarify whether the protocol involved the randomization of children and infants.

(8) HHS regulations at 45 CFR 46.110(b)(1) limit the use of expedited review procedures to specific research categories published in the Federal Register. OHRP is concerned that:

(a) The IRB inappropriately confounds the concepts of minimal risk and expedited review. UW procedures state that IRB review of proposed changes may be expedited if they are "minimal risk changes" but not if "changes involve more than minimal risk." The regulations refer to "minor changes" being reviewed in an expedited manner.

(b) Use of expedited review by the IRB has not been restricted to the categories published in the Federal Register. OHRP recommends that documentation for initial and continuing reviews that are conducted utilizing expedited review procedures include citation of the specific permissible categories (see 63 FR 60364) justifying the expedited review.

Please respond.

Please submit to OHRP your response to the above findings, questions and concerns no later than June 20, 2001. If upon further review of the above concerns and questions, UW identifies additional instances of non-compliance with the HHS regulations for protection of human subjects, please include detailed corrective action plans to address the noncompliance.

OHRP appreciates your institution's continued commitment to the protection of human research subjects. Do not hesitate to contact me if you have any questions regarding this matter.

Sincerely,

Kristina C. Borror, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Zane Brown, Chair, Biomedical IRB, UW
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