DEPARTMENT OF HEALTH & HUMAN SERVICES

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June 11, 2001

William H. Parker
Vice Chancellor for Research
155 Administration Building
University of California, Irvine
Irvine, CA 92697-3175

RE: Human Research Protections Under Multiple Project Assurance (MPA) # 1305
Research Projects: Evaluation of Pulse Oximeters

Dear Mr. Parker:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR) has reviewed your April 21, 2000 report regarding the above referenced research that was submitted in response to OPRR's March 22, 2000 letter. OHRP apologizes for its delay in responding to your report.

Based on its review, OHRP makes the following determinations:

(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 finds that the required findings for waiver or alteration of informed consent were not made when research project HS #94-215, which involved waiver of informed consent, was approved.

(2) HHS regulations at 45 CFR 46.109(a) require that the IRB review and approve, require modifications in, or disapprove, all human subject research, unless the research is exempt under HHS regulations at 45 CFR 46.101(b). OHRP finds that subjects were enrolled in research project HS #94-215 prior to IRB approval of this project.

Required Action: Please provide OHRP a copy of the findings and recommendations of the IRB subcommittee performing a review of this matter, and any subsequent corrective actions taken by the IRB. Please forward your report so that OHRP receives it no later than July 31, 2001. OHRP acknowledges that since review of this research was conducted, additional IRB staff have been hired and additional training and education of staff and investigators have been implemented.

OHRP has the following additional questions and concerns.

(3) OHRP is concerned that the informed consent documents reviewed and approved by the IRB for HS #93-384 failed to adequately address the following elements required by HHS regulations at 45 CFR 46.116(a):

(a) Section 46.116(a)(1): (i) the expected duration of the subject's participation; and (ii) a description of the procedures to be followed. The protocol and publications resulting from this research described the following procedures which are not mentioned in the informed consent document:

- How subjects would be "exposed to decreasing oxygen concentrations."
- Amount of blood drawn.
- Subjects were provided a rubber mouthpiece that created a seal and prevented subjects from breathing room air and had their noses tightly clamped with a pin to prevent room air breathing.

(b) Section 46.116(a)(2): A description of any reasonably foreseeable risks and discomforts. The informed consent document did not mention the following: (i) consequences of occurrence of any of the risks nor their treatment; and (ii) possible adverse reaction to lidocaine (the IRB removed mention of lidocaine use from the informed consent document.)

Please respond.

(4) HHS regulations at 45 CFR 46.116 require that the information that is given to subjects must be in language understandable to the subject. OHRP is concerned that the informed consent document approved by the IRB for HS #93-384 appeared to include complex language that would not be understandable to all subjects. Please respond.

(5) The approval letter for HS #94-215 dated 6-27-95 stated that the protocol had received review by the full board. However, other IRB documents indicated that this protocol was reviewed in an expedited manner and no IRB minutes were provided for this protocol. Please clarify. OHRP recommends that documentation for initial and continuing reviews conducted utilizing expedited review procedures include the specific permissible categories (see 63 FR 60364) justifying the expedited review.

(6) 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. Initial review for HS #94-215 occurred on 6-6-94, and continuing review occurred on 6-27-95. The protocol was not closed until 02-05-98; however, this protocol was not reviewed again after 6-27-95. Please respond. OHRP acknowledges that no subjects were enrolled in the research after 07-06-94.

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.
Compliance Oversight Coordinator
Division of Human Subject Protections

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