**DEPARTMENT OF HEALTH & HUMAN SERVICES**

**Office of the Secretary**
**Office of Public Health and Science**

**Office for Human Research Protections**
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August 1, 2008

Jeffrey M. Cheek, Ph.D.
Associate Vice Provost for Research Compliance and Operations
University of Washington
Office of Research
G 80 Gerberding Hall Box 351202
Seattle, WA 98195-1202

**RE: Human Research Subject Protections Under Federalwide Assurance FWA- 6878**

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|---|---|
| **Research Project:** | Hypertonic Saline Study |
| **Principal Investigator:** | Eileen Bulger, M.D. |
| **Research Project:** | Prehospital Resuscitation using an IMpedance valve and Early vs. Delayed analysis – ROC PRIMED |
| **Principal Investigator:** | Peter J. Kudenchuk, MD |

Dear Dr. Cheek:

Thank you for your October 10, 2007 report in response to our August 2, 2007 letter regarding research conducted under the above-referenced research projects. Based on the information submitted to us, we make the following determinations:

## A. Determination Regarding the Above-Referenced Research

1. Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(b)(4)(iii) require that the institutional review board (IRB) review and approve all proposed changes in a research activity, during the period for which IRB approval has already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. A complainant alleged that the University of Washington (UW) IRB did not review and approve changes to the protocols referenced above prior to initiation of such changes. In specific, a complainant alleged that the above-referenced research protocols provided that individuals, who did not want to participate in the research, could opt out of the research by requesting a MedicAlert-type bracelet. According to the complainant,

investigators were giving individuals a rubber bracelet with "no study" being written in with pen in lieu of the protocol-specified MedicAlert-type bracelet.

Based on the documentation provided in your October 10, 2007 report, we have determined that the allegation of noncompliance is unproven. No evidence was presented to us indicating that there was a violation of HHS regulations at 45 CFR 46.103(b)(4)(iii). In fact, we reviewed the UW IRB file for the Hypertonic Saline Study (hypertonic study) and discovered that the initial proposed protocol contained an "opt-out" provision involving MedicAlert-type bracelets. However, during the initial review the UW IRB rejected the idea of "opt-out" bracelets because the UW IRB believed that the "opt-out" provision is only valid if the investigator is assured that every person who would like to opt-out has that opportunity. The UW IRB determined that the investigator for the hypertonic study could not be assured that everyone in the target locales would know about the study; thus, on July 17, 2006, the UW approved a hypertonic study protocol that did not contain any "opt-out" procedure. Subsequently, the investigator requested that the hypertonic study protocol be modified to include an "opt out" provision for persons wishing to be excluded from the study. The proposed "opt out" provision included the dissemination of stainless steel MedicAlert-type bracelets. This modification was approved by the UW IRB on May 30, 2007. Shortly after the May 30, 2007 IRB approval (i.e., in a June 7, 2007 modification request form) the investigator informed the UW IRB that the UW IRB-approved stainless steel MedicAlert-type bracelets would not be available for approximately 10 days. Thus, the investigator proposed to use red rubber bracelets with the wording "No ROC study," written in black indelible ink, until the stainless steel MedicAlert-type bracelets were available. The UW IRB approved this modification request on June 7, 2007. Thus, the facts show that the use of the rubber bracelet with black ink writing was approved by the UW IRB at the time the complaint was made to OHRP in June 2007.

Moreover, we reviewed the UW IRB file for the Prehospital Resuscitation using an IMpedance valve and Early vs. Delayed analysis – ROC PRIMED (ROC PRIMED study) and discovered that on April 4, 2007, the UW IRB approved a ROC PRIMED study protocol that did not contain an "opt out" provision. Subsequently, the investigator requested that the hypertonic study protocol be modified to include an "opt out" provision for persons wishing to be excluded from the study. The proposed "opt out" provision included the dissemination of stainless steel MedicAlert-type bracelets. This modification was approved by the UW IRB on May 30, 2007. Shortly after the May 30, 2007 IRB approval (i.e., in a June 7, 2007 modification request form) the investigator informed the UW IRB that the UW IRB-approved stainless steel MedicAlert-type bracelets would not be available for approximately 10 days. Thus, the investigator proposed to use red rubber bracelets with the wording "No ROC study," written in black indelible ink, until the stainless steel MedicAlert-type bracelets were available. The UW IRB approved this modification request on June 7, 2007. Thus, the facts show that the use of the rubber bracelet with black ink writing was approved by the UW IRB for the ROC PRIMED study as well at the time the complaint was made to OHRP in June 2007.

## B. Questions and Concerns Regarding the Hypertonic Study

1. [Redacted]

2. [Redacted]

[Redacted]

3. [Redacted]

4. [Redacted]

5. [Redacted]

[Redacted]

6. [Redacted]

[Redacted]

6. [Redacted]

## C. Questions and Concerns Regarding the ROC-PRIMED Study

1. [Redacted]

## D. Questions and Concerns Regarding UW's System for Protecting Human Subjects

1. [Redacted]

2. [Redacted]

Please provide us with responses to the above questions and concerns by September 5, 2008. Please don't hesitate to contact me if you need assistance in developing your corrective action plan.

We appreciate your institution's continued commitment to the protection of human research subjects.

Sincerely,

Lisa A. Rooney, J.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Karen E. Moe, Ph.D., Director, Human Subjects Division, University of Washington

Dr. Zane A. Brown, Chair, IRB #1A, University of Washington
Dr. Alan J. Wilensky, Chair, IRB #2B, University of Washington
Dr. Patricia C. Kuszler, Chair, IRB #3C, University of Washington
Dr. Margaret J. Neff, Chair, IRB #4D, University of Washington
Dr. Carl Rimmele, Chair, IRB #5G, University of Washington
Dr. Donald J. Sherrard, Chair, IRB #6V, University of Washington
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Ms. Sherry Mills, Office for Extramural Research, National Institutes of Health
Mr. Joe Ellis, OER, NIH
Dr. Andrew C. von Eschenbach, Commissioner, Food and Drug Administration
Dr. Joanne R. Less, FDA
Dr. Laurence Landow, FDA