DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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December 13, 2006

Jeffrey M. Cheek, Ph.D.
Associate Vice Provost for Research
Compliance and Operations
Office of Research
University of Washington
G80 Gerberding Hall
Seattle, WA 98195-1202

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

| | |
|---|---|
| **Research Project:** | **Casa Pia Study of Dental Amalgams in Children** |
| **Principal Investigator:** | **Dr. Timothy A. DeRouen** |
| **IRB Number:** | **95-0401-A/C 10** |
| **HHS Project Number:** | **5U01DE011894** |

Dear Dr. Cheek:

The Office for Human Research Protections (OHRP) has reviewed the University of Washington's (UW) October 6, 2006 report that was submitted in response to OHRP's August 29, 2006 letter regarding the above-referenced research.

Based on its review of your October 6, 2006 and August 29, 2005 reports, OHRP makes the following determination:

> It was alleged that the informed consent documents for the above-referenced research failed to provide an adequate description of the reasonably foreseeable risks and discomforts of the research, as required by Department of Health and Human Services regulations at 45 CFR 46.116(a)(2). In specific, it was alleged that the risks of dental amalgam were not adequately described in the informed consent document.
>
> > (1) Regarding the placement of dental restorations, OHRP notes that the IRB-approved informed consent document for the above-referenced research states:

(a) "None of these examinations, treatments or tests are experimental. They are all procedures which are commonly in use throughout the world. The only risks or discomforts from these procedures are the ones usually associated with routine dental care or with routine medical examinations or tests."

(b) "When the dental examination, cleaning, and treatment are performed, there may be slight discomfort from time to time, and your child will feel pressure in his/her mouth. Local anesthesia to numb the teeth and gums (lidocaine, carbocaine) will always be used whenever indicated to keep any discomfort from occurring. This anesthesia (numbing) is given by first applying cream (topical anesthesia) which numbs the gum, and then injecting a small amount of liquid into the gum near the teeth. Although many of these injections are painless, there may be an occasional small stinging feeling. There is a very small chance of an allergic reaction to the anesthetics used for dental care. The reaction to the topical anesthetic would probably show up as a reddened area at the sire of application. This should pass within a day."

(2) Documents provided with UW's October 6, 2006 report stated:

(a) "The purpose of this study is to define the risks of two standard-of-care procedures. The study falls under the minimal risk guidelines spelled out in 45 CFR 46.404 in that the research does not involve greater than minimal risk, defined as the probability and magnitude of harm or discomfort anticipated in the research are not greater in an of themselves than those normally encountered in daily life or during the performance of routine physical or psychological examinations."

(b) "Given that the study has met the conditions for minimal risk and involves standard-of-care procedures the committee felt that it was not necessary for the consent form to discuss potential risks from these standard-of-care procedures."

OHRP finds that the informed consent document for the above-referenced research failed to adequately describe the reasonably foreseeable risks of amalgams and composite materials used in the dental procedures.

**Required Action:** By February 9, 2007, please provide OHRP with a satisfactory corrective action plan to address the above determination.

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,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Karen Moe, Acting Director, Humans Subjects Division, UW
Dr. Zane Brown, Chair Human Subjects Committee A, UW
Dr. Alen Wilenski, Chair Human Subjects Committee B, UW
Dr. Patricia Kuszler, Chair Human Subjects Committee C, UW
Dr. Rebekah Rein, Chair Human Subjects Committee D, UW
Dr. Carl Remmele, Chair Human Subjects Committee G, UW
Dr. Donald Sherrard, Chair Human Subjects Committee V, UW
Dr. Deborah McCutchen, Chair Human Subjects Committee J, UW
Commissioner, FDA
Dr. Linda Tollefson, FDA
Dr. Norris Alderson, FDA
Dr. Sam Shekar, NIH
Dr. Bernard Schwetz, OHRP
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Ms Shirley Hicks, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Carla Brown, OHRP