



Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 240-453-8298
FAX: 240-453-6909
E-mail: patrick.mcneilly@hhs.gov

August 29, 2006

Mary E. Lidstrom, Ph.D.
Vice Provost for Research
Office of Research
University of Washington
G80 Gerberding Hall
Seattle, WA 98195

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

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

Dear Dr. Lidstrom:

The Office for Human Research Protections (OHRP) has reviewed the University of Washington's (UW) August 29, 2005 report that was submitted in response to OHRP's July 25, 2005 letter regarding the above-referenced research.

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

(1) It was alleged that researchers in the above-referenced research failed to minimize risks to subjects, as required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.111(a)(1). In specific it was alleged that the research continued despite new scientific findings that emphasized the potential for harm from doses of mercury within the range of that received by the general population from amalgam fillings. OHRP finds that this allegation could not be substantiated. In particular, OHRP notes that the interventions utilized in the research involved standard materials and techniques used in dental restorations. In addition, the study was reviewed by a Data Safety and Monitoring Board which apparently did not identify any new scientific

findings related to potential harm to subjects or question the continuation of the study.

(2) It was alleged that inappropriate advocates were appointed for wards enrolled in the above-referenced research, as required by HHS regulations at 45 CFR 46.406 or 46.407. OHRP finds that this allegation could not be substantiated. In particular, OHRP notes that the UW institutional review board (IRB) determined that the above-referenced research met the conditions for approval under 45 CFR 46.404 and as a result the appointing of an advocate for the subjects who were wards of the state was not required.

(3) It was alleged that the informed consent document for the above-referenced research failed to include an appropriate description of any benefits to the subjects or to others that may reasonably be expected from the research, as required by HHS regulations at 45 CFR 46.116(a)(3). In specific, it was alleged that the benefits of the research may be overstated.

OHRP finds that this allegation could not be substantiated. In particular, OHRP notes that an August 22, 2005 letter from the UW IRB chair and IRB administrator to Dr. Timothy DeRouen states:

(a) "We note that the children of the Casa Pia Schools would have received some institutional dental care regardless of the study. We also note that all children screened for the study were still provided with comprehensive dental care by the study even if found to be ineligible for the study."

(b) "It is our determination that all children at the school within a specific age range had an opportunity to be screened for enrollment in the study. Regardless of enrollment all of these children were given dental care by the study. This dental care was equivalent to US standard-of-care. Therefore the dental benefit of being in the study is the equivalent to the dental benefit of screening out of the study."

At this time, OHRP has the following additional question:

(4) [Redacted]

Please provide your response to the above question no later than October 6, 2006.

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: Ms. Helen McGough, 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
Commissioner, FDA
Dr. David Lepay, FDA
Dr. Norris Alderson, FDA
Dr. Sam Shekar, NIH
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Dr. Kristina Borrer, OHRP
Dr. Irene Stith-Coleman, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Carla Brown, OHRP