DEPARTMENT OF HEALTH & HUMAN SERVICES
Office of the Secretary
Office of Public Health and Science

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

Telephone: 240-453-8132
FAX: 240-453-6909
E-mail:Kristina.Borror@hhs.gov

September 24, 2007

Chiyome L. Fukino, MD
Director of Health
Hawaii State Department of Health
1250 Punchbowl Street
Honolulu, HI 96813

James R. Gaines, Ph.D.
Vice President for Research
University of Hawaii
2444 Dole Street
Honolulu, HI 96822

RE: Human Research Protections Under Federalwide Assurance FWA-3526 and FWA-118

Research Project: Effects of Upcountry Maui Water Additives on Health
Principal Investigator: Amber Rohner; Kenton Kramer, Ph.D., supervising professor

Dear Drs. Fukino and Gaines:

The Office for Human Research Protections (OHRP) has reviewed the Hawaii State Department of Health's (HSDOH) July 24, 2007 and the University of Hawaii's (UH) July 23, 2007 responses to OHRP's June 25, 2007 letter regarding compliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46).

In its June 25, 2007 letter, OHRP made the following determination:

(1) OHRP found that the HSDOH IRBs did not have written IRB procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5):

(a) The procedures which the IRB will follow for determining which projects require review more often than annually.

(b) The procedures which the IRB will follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review.

(c) The procedures which the IRB will follow for ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(d) The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, any department or agency head, and OHRP of: (i) any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and (ii) any suspension or termination of IRB approval.

Corrective Action: OHRP acknowledges that HSDOH has revised its written IRB procedures to include the above activities. OHRP finds that the corrective actions adequately address the finding, and are appropriate under your FWAs. As a result, OHRP anticipates no further involvement in this matter.

OHRP has the following additional recommendations:

(2) OHRP acknowledges HSDOH's statement that the HSDOH IRB reviews HHS grant applications and the UH's statement that grant applications are submitted as part of the application process. Please note that OHRP can find no information in your written IRB procedures or IRB application forms indicating that this is the case. OHRP recommends that the written IRB procedures and IRB application forms be revised to discuss IRB submission and review of HHS grant applications involving human subjects research.

(3) OHRP acknowledges HSDOH's statement that the "Policies and Standard Operating Procedures for the Hawaii State Department of Health Institutional Review Board" which was published by the Center for Clinical Research Practice in 2002 was a draft document circulated for comments, but was not adopted. The Hawaii Department of Health Policies and Procedures Governing Research Involving Human

Subjects were adopted May 27, 2005 instead. It appears that some HSDOH investigators have not received the Hawaii Department of Health Policies and Procedures Governing Research Involving Human Subjects; OHRP recommends that all human subjects research investigators receive a copy of these written IRB procedures.

(4) OHRP notes that the definitions of "Research" and "Human Subject" in the Hawaii Department of Health Policies and Procedures Governing Research Involving Human Subjects that purport to be as "defined in the federal regulations" are incomplete. OHRP recommends that the complete definitions be included.

(5) OHRP notes that pages 22-23 of the Hawaii Department of Health Policies and Procedures Governing Research Involving Human Subjects states that when "non-compliance is found to be serious in nature, the IRB may….report to the sponsor, administrative officials, and government agencies (e.g., OHPR [sic], FDA, etc.)" Similarly, on page 23 of the manual it states "The … IRB Institutional Official may send written notice on behalf of the IRB to the following entities, as required under Federal regulations: the OHRP; the OHRP and FDA as applicable, if the matter involves the non-submission of a project which should have been reviewed by the CHS, and the researcher's failure to do so has resulted in unanticipated risks to human subjects or serious or continuing Non-Compliance with IRB requirements; external and internal sponsors funding a study under suspension." Please note that these are regulatory requirements and therefore the "may" in each of these statements should be changed to "must."

(6) Pages 43-44 of the manual state that a grace period can be approved by the IRB chair for studies that have not undergone review at least annually "when closure may cause risk to the human subject(s), if there is an extenuating circumstance, or to allow for the submission and receipt of required documentation for the CHS review process." OHRP previously noted that the only circumstances that would permit research to continue beyond the date the approval expired are when it is in the best interest of the subject(s) to continue. UH responded "the additional language is intended to be able to also appropriately handle situations that, despite providing expiration notices and other measures to have all continuing review dates met, [sic] occasionally occur because of sabbaticals and other circumstances. In these rare cases, the committee's [sic] review the projects at the earliest opportunity. In all but very rare times, these are social science/behavioral projects of relatively low risk, usually approved under expedited review and there was no actual activity going on during the lapsed period." OHRP notes that if there is no actual activity going on during the lapsed period, then there should be no problem with stopping research activity during a lapse of approval. Factors such as provision of expiration notices, sabbaticals, level of risk, and initial approval in an expedited manner are irrelevant in determining whether or not it is in the best interest of the subject(s) to continue.

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.
Director
Division of Compliance Oversight

cc:

Dr. Betty J. Wood, Human Subjects Administrator, Hawaii State Department of Health
Dr. Catherine A. Sorensen, IRB Chairperson, Hawaii State Department of Health
Mr. William H. Dendle, Executive Secretary/Compliance Officer, University of Hawaii Committee on Human Studies
Dr. Peter V. Garrod, IRB Chairperson, University of Hawaii IRB #1
Dr. Dennis McDougall, IRB Chairperson, University of Hawaii IRB #2
Dr. Kenton Kramer, University of Hawaii
Dr. Lorrin Pang, Hawaii State Department of Health
Dr. Ivor Pritchard, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Ms. Patricia El-Hinnawy, OHRP
Ms. Kelley Booher, OHRP
Mr. Barry Bowman, OHRP