



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
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Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
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May 17, 2007

Re: Animal Welfare Assurance
A3196-01 [OLAW Case 3M]

Roberto Peccei, Ph.D.
Vice Chancellor for Research
Office of the Chancellor
University of California-Los Angeles
405 Hilgard Avenue
Los Angeles, CA 90024-1405

Dear Dr. Peccei,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your May 7, 2007 letter of a final report concerning an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of California, Los Angeles (UCLA) after the initial report via a phone call to this Office on February 28, 2007 by Ms. Kathy Wadsworth. According to the information provided, OLAW understands that an attending veterinarian suspended research activities on a project due to unexpected post-surgical deaths of rabbits. The suspension of the surgical activities was later supported by the Animal Research Committee (ARC) at a convened meeting pending the results of an investigation. Other portions of the protocol continued including monitoring for complications and tissue harvest.

Corrective actions consisted of collaboration between the PI and veterinary staff to develop the following recommendations that are to be included in a protocol modification:

- 1) Use of a fentanyl patch for improved and sustained pain control.
- 2) Subcutaneous injections of Baytril.
- 3) Implementation of a feeding/dietary log and diet supplementation for rabbits with poor appetite.
- 4) Gram staining of urine.
- 5) Pre and Post-operative blood work.
- 6) Shaving a larger ventral area of the animal prior to surgery to help prevent urine scalding of the skin.

OLAW understands that the ARC lifted the suspension on March 12, 2007 and that the protocol involved was not PHS supported, but concurs that the incident warranted reporting. The establishment and application of policies and practices that are consistent with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals at UCLA are commendable and avoid the perception of a double standard. We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

Brent C. Morse, DVM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: Dr. William McBride, IACUC Chair

Ms. Kathy I. Wadsworth, Associate Director - Animal Subjects Research

Box 951405
Los Angeles, CA 90095-1405
phone: 310-825-7943
fax: 310-206-6030
rpeccei@conet.ucla.edu

May 7, 2007

Axel V. Wolff, M.S., D.V.M.
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

RE: Final Report of Suspension of Activities
Animal Welfare Assurance A3196-01

Dear Dr. Wolff:

I am writing to provide you with a final report regarding a suspension of activities, which was initially reported to you by Associate Director Kathy Wadsworth on February 28, 2007, in accordance with PHS Policy IV.C.8¹. The incident involved unexpected deaths following surgical reconstruction experiments described in the approved protocol. The protocol was not supported by federal funds. The study involved USDA-covered species (rabbits). As such, an initial report of the suspension was also provided to the USDA on February 28, 2007.

As Ms. Wadsworth informed you on February 28, 2007, the Chancellor's Animal Research Committee (ARC) was notified that an attending veterinarian for the Division of Laboratory Animal Medicine (DLAM) suspended research activities for the project pending an investigation regarding the unanticipated animal deaths occurring in this study².

¹ PHS Policy IV.C.8. "If the IACUC suspends an activity involving animals, the Institutional Official in consultation with the IACUC shall review the reasons for suspension, take appropriate corrective action, and report that action with a full explanation to OLAW"

² ARC Policy on Authority of the Attending Veterinarian. "The attending veterinarian may immediately stop research activities conducted under a protocol for humane reasons or protocol deviations pending ARC review of an incident."

The ARC reviewed the initial veterinary report regarding this matter at the convened meeting of February 26, 2007, at which time the Committee voted to continue the suspension of surgical activities until the investigation had concluded and the results of the investigation were reviewed at a convened ARC meeting. The Committee also determined that animals that had already been surgicated must be maintained in accordance with the approved protocol and monitored for complications which would warrant premature euthanasia. Additionally, tissues could be harvested as described in the approved protocol, and be made available to DLAM veterinary staff as requested for the purpose of the aforementioned investigation.

A meeting was held March 5, 2007 between the Principal Investigator and DLAM veterinary staff to discuss the necropsy findings, as well as to outline a strict monitoring regimen in order to minimize the likelihood of future animal deaths. In summary, the protocol involves the segmental replacement of a portion of the rabbit penile urethra with either a biodegradable graft, graft seeded with autologous smooth muscle cells derived from adipose stem cells, or a segment of the rabbit's own native urethral (sham group). It was clear to the investigator that greater complications arose in the graft groups. Upon further review of the research findings in this group, six of eight rabbits developed urethral strictures with likely progressive stricture development over longer time points. The poor outcomes in this group may have been secondary to stricture-related sequelae, though necropsy could not confirm this. It was also noted that the rabbits had increased loss of appetite in the immediate postoperative period, which resolved following removal of e-collars and urinary catheters.

The recommendations of the Principal Investigator and veterinarians were provided to the ARC for review at the convened meeting of March 12, 2007. The Committee found the proposed modifications to ensure optimal outcomes and to limit the risk of unanticipated adverse events to be reasonable and appropriate. As such, the ARC lifted the suspension of the study, pending the investigator's continued collaboration with DLAM veterinary staff, and submission of a revised protocol amendment containing the following proposed modifications:

1. Employment of a fentanyl patch to be applied starting preoperative day 1 and extending into the postoperative period for improved and sustained pain control. It was thought that Fentanyl would cause less appetite suppression than buprenorphine.
2. As the rabbits had decreased oral intake in the postoperative period, subcutaneous injections of Baytril twice daily should be given for a total of 10 days postoperatively, extending 3 days beyond the time when urinary catheters are removed.

3. A daily feeding/dietary log should be maintained on each rabbit and the diets of those rabbits with poor appetite supplemented with treats as well as yogurt-covered pellets.
4. Gram staining of urine to assess for bacterial content at several postoperative time points.
5. Blood work to include a CBC and/or chemistries, to be obtained preoperatively as well as 2 weeks and 4 weeks postoperatively.
6. The ARC also recommended shaving a larger ventral area of the animals prior to surgery, to help prevent urine scalding of the skin.

If you have any questions or concerns, please do not hesitate to contact me at (310) 825-7943.

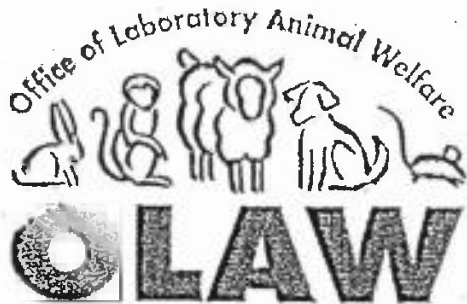
Sincerely,

A handwritten signature in black ink, appearing to read 'Roberto Peccei', written in a cursive style.

Roberto Peccei
Vice Chancellor for Research

cc: Professor William H. McBride, Chair, ARC
Judith L. Brookshire, Director, OPRS
Kathy Wadsworth, Associate Director, Animal Subjects Research

A31965M



Initial Report of Noncompliance

Date: 2/23/07

Time: PM

Name of Person reporting: Kathy Wadsworth
 Telephone #: 310 825 5227
 Fax #:
 Email:

Name of Institution: U of California - Los Angeles
 Assurance number: A3196

Did incident involve PHS funded activity? No
 Funding component: _____
 Was funding component contacted (if necessary): _____

What happened?
 - Svs pending protocol due to unexpected deaths
 Not due to negligence, Surgery performed

Species involved: Rabbits
 Personnel involved:
 Dates and times:
 Animal deaths: Yes

Projected plan and schedule for correction/prevention (if known): _____
 Pathology underway to determine cause of deaths

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY
 Case # _____

