

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

February 7, 2008

Brent C. Morse, DVM
Animal Welfare Program Specialist
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

RE: Report of Noncompliance (as referenced in – OLAW Case 3V)
UCLA's Animal Welfare Assurance #A3196-01

Dear Dr. Morse:

Thank you again for your correspondence dated November 28, 2007 regarding OLAW Case 3V. The Chancellor's Animal Research Committee (ARC) appreciates your thorough review of the report and is grateful for your comments and suggestions regarding the Committee's actions regarding the principal investigator's history of noncompliance. As noted in our January 31, 2008 correspondence, imprecise wording was employed in our November 6, 2007 correspondence to describe why the October 10, 2005 incident was not reported to OLAW. Various factors occurring at that time resulted in the failure of ARC staff to carry-out the usual incident follow-up.

At this time, I wish to ask you to accept the following detailed report pertaining to this matter. At the time of the incident, the project received funding from various sources, including NIH grant #P50-CA86306, NIH grant #NS-38489, NIH/NCI grant #441458/HW/33689, NIH grant #P50-CA092131, NIH/NCI grant #NR01-CA107166, DOD grant #PC031130.

The ARC was notified on October 6, 2005 by UCLA's Division of Laboratory Animal Medicine (DLAM) veterinary staff of continued failure of the investigator to respond to DLAM requests to treat or euthanize animals, as follows:

- September 2, 2005: Veterinary staff sent a health case notification to the PI to treat or euthanize mice with abdominal distention and palpable mass. As veterinary staff did not receive a response to the notification, DLAM staff euthanized the animals.

FEB 14 '08 AM 7:09

- September 13, 2005: Veterinary staff sent a health case notification to the lab to euthanize or treat a mouse exhibiting hunched posture and ruffled coat. Again, veterinary staff did not receive a response, and DLAM staff subsequently euthanized the animal.
- September 26, 2005: Veterinary staff sent a health case notification to the PI to euthanize or treat a mouse that sustained injuries to the tail and caudal body, likely due to fighting. DLAM did not receive a response to the notification. therefore the animal was euthanized.
- October 4, 2005: Veterinary staff sent a health case notification to the PI to euthanize or treat a mouse that sustained injuries to the lower back, likely due to fighting. DLAM again received no response to the notification. DLAM staff subsequently euthanized the animal.

On October 10, 2005, Associate Director Kathy Wadsworth forwarded an initial query into the incident to the PI. In accordance with the ARC Policy, Investigating Allegations of Mistreatment or Other Noncompliance Issues¹, the PI was given an opportunity to respond to the allegation of noncompliance, and if appropriate, to provide a corrective action plan to avoid such violations from occurring in the future. The PI was also reminded of the ARC Policy on Notification of Investigators Regarding Sick or Injured Animals which states that *"failure of research personnel to carry out veterinary orders is considered a serious violation reportable to the NIH Office of Laboratory Animal Welfare."*² *It is unacceptable to simply fail to respond to such notification and expect DLAM staff to treat or euthanize the animal."*

Ms. Wadsworth was informed the same day (October 10, 2005) that the PI "personal" Additionally, a representative from the PI's lab informed the veterinarian reporting the incident that the fight wounds referenced in the October 4, 2005 report had healed on their own, and that DLAM did not euthanize the animal as reported in the October 10, 2005 initial query. The reporting veterinarian acknowledged the error in the October 10, 2005 initial query, but reminded the lab that though the wounds had healed on their own, the incident was still considered a violation because the lab had failed to follow veterinary orders to initiate treatment. The veterinarian reminded the PI's staff to "make sure everyone in the lab knows – that some action must be taken within 24 hours of the date/time stamp on the notification case emails from us."

¹ ARC Policy on Notification of Investigators Regarding Sick or Injured Animals: "In every investigation, the person(s) against whom the complaint has been raised shall be given notice of the concern and provided an opportunity to address the allegations in writing."

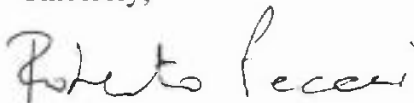
² OLAW Notice #NOT-OD-05-034: Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals (available at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-034.html>)

The veterinarian reporting the incident to the ARC suggested that since the PI had been out of the country due to personal / perhaps "the Committee would take that – and the size of [the PIs'] lab – into consideration." Upon the PI's return to her lab, DLAM staff met with the PI and her staff to discuss the above incidents, and suggest improved monitoring and endpoints for the mice.

As Institutional Official for UCLA, I support the Committee and accept responsibility for the delay in reporting this incident of noncompliance. The ARC takes its charge seriously and endeavors to enhance its process for investigating and resolving all noncompliance with federal, local and institutional regulations, policies and guidelines.

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

Sincerely,



Roberto Peccei
Vice Chancellor for Research

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



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive - MSC 7982
Bethesda, Maryland 20892-7982
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
Facsimile: (301) 402-2803

February 14, 2008

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

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 January 31 and February 7, 2008 letters responding to our request for additional information 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). According to the information provided, OLAW understands that the Chancellor's Animal Research Committee (ARC) has determined that additional, specific supplemental training techniques for the PI's lab will be implemented prior to March 2008 and that the veterinary staff will report back to the ARC regarding the success of this action.

It is also understood that the ARC examined past issues concerning this PI and laboratory and has reported that between September 2, 2005 and October 4, 2005 the lab in question failed to respond in a timely manner to health case notifications from the veterinary staff resulting in the veterinary staff subsequently euthanizing animals in three of the referenced incidents. It is further understood that at the time of the incidents, the PI was personal and that subsequent to her return the Department of Laboratory Animal Medicine met with her and her staff to improve monitoring and endpoints for the mice.

OLAW appreciates the University of California, Los Angeles' considerations of these matters. This Office believes it is important to document current and past incidents of noncompliance with the Policy and encourages all assured institutions to report them whenever they are discovered. Similarly, the actions taken to resolve the issues and prevent recurrences were appropriate. We appreciate being informed of these matters 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 L. Wadsworth, Associate Director - Animal Subjects Research

UCLA

UNIVERSITY OF CALIFORNIA,
LOS ANGELES

ROBERTO PECCEI
Vice Chancellor for Research

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

January 31, 2008

Brent C. Morse, DVM
Animal Welfare Program Specialist
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

RE: Response to OLAW Letter of November 28, 2007, Regarding a Report of Noncompliance – OLAW Case 3V (Animal Welfare Assurance A3196-01)

Dear Dr. Morse:

Thank you for your correspondence dated November 28, 2007 regarding OLAW Case 3V. The Chancellor's Animal Research Committee (ARC) appreciates your thorough review of the report and is grateful for your comments and suggestions regarding the Committee's actions regarding the principal investigator's history of noncompliance.

As requested, the ARC re-examined Case 3V at the convened meeting of December 17, 2007. During the discussion, the Committee reviewed the previous issues, including the October 10, 2005 incident, and subsequent attempts to improve compliance in the PI's lab, as described in the ARC's report of November 6, 2007. The Committee had the following comments:

Appointment of a more experienced and/or responsive PI or Co-PI:

The Committee notes that the PI is a leading authorities in her field. As such, it would not be reasonable or advisable to appoint another PI to oversee the animal work. The scope and nature of the research conducted in the PI's laboratory, including the creation of genetically engineered animal models for human diseases, and evaluation of these models for embryogenesis, hematopoiesis, neurogenesis, and tumorigenesis, is

complex and groundbreaking, for which definitive endpoints have not been well established. Some animals die unexpectedly without warning, making it often difficult for the PI and her lab staff to monitor such events.

Over the past several years, the PI has worked in collaboration with veterinary staff from UCLA's Division of Laboratory Animal Medicine (DLAM) to improve the endpoints and identify the cause of lethal phenotypes. This collaboration has resulted in fewer such animal deaths without euthanasia; however, as the scope of the investigator's research is extensive and the number of staff she oversees is quite large, the ARC determined that additional measures are warranted to improve staff understanding of the endpoints, as well as to enhance monitoring of these animals.

It was noted that lab managers from other large animal laboratories employ supplemental training techniques such as protocol questionnaires, quizzes, and adjunct training that has resulted in dramatic improvements in compliance. As such, Associate Director Kathy Wadsworth will arrange for the PI to consult with one of these lab managers to develop a customized training program for her staff. The meeting will take place within the next two months and the new training techniques will be implemented prior to March 2008. Veterinary staff will report back to the ARC regarding the success of the supplemental training techniques.

Prior incidents which may have been reportable to OLAW:

Because this recent incident involved deviations from the PI's approved protocol pertaining to the use of a biohazardous agent (Tamoxifen), this matter received close ARC scrutiny. It was noted that previous incidents involved failure of staff to euthanize mice prior to death. As noted above, DLAM veterinary staff have collaborated with the PI to improve the monitoring and identify the cause of lethal phenotypes.

NIH Guidance NOT-OD-05-034 lists the following as examples of situations not normally required to be reported:

- Animal death or illness from spontaneous disease when appropriate quarantine, preventative medical, surveillance, diagnostic, and therapeutic procedures were in place and followed:
- Animal death or injuries related to manipulations that fall within parameters described in the IACUC-approved protocol.

Though the ARC does not report animal deaths that fall within the parameters described in an investigator's approved protocol, the ARC does report animal deaths when investigators and laboratory staff fail to carry out veterinary orders (see attached *ARC Policy on Notification of Investigators with Sick or Injured animals*). In the October 10, 2005 incident, the PI and her lab staff were notified of four (4) separate instances in which mice with observable illness were not euthanized as directed by DLAM veterinary staff. As such, this normally would have been reported to OLAW as a noncompliance.

However, as the PI was [redacted] *personal* /ARC representatives were not able to meet with the PI in a timely fashion to discuss the incident and develop an effective corrective action plan.

I wish to clarify at this time that imprecise wording was employed in the November 6, 2007 correspondence to describe why the October 10, 2005 incident was not reported to OLAW ("At that time, it was noted that the PI was [redacted] *personal*). As such, this incident was not reported to the NIH/OLAW"). The reason that this event was not reported to OLAW was likely due to a combination of factors occurring at the time of the incident, which resulted in the failure of ARC staff to [redacted] *personal* at the usual incident follow-up (e.g., Associate Director Kathy Wadsworth's [redacted] *personal*, 2005; prolonged inability of the ARC to contact the PI who was [redacted] *personal*). As acknowledged in the ARC's November 6, 2007 report to OLAW, the members agreed that it was regrettable that the incident was not reported prior to this most recent incident.

The ARC takes its charge seriously and endeavors to enhance its process for investigating and resolving all noncompliance with federal, local and institutional regulations, policies and guidelines. We believe that the ARC and investigators share a collective responsibility for the ethical conduct of research at UCLA. This collaboration exists by upholding the highest ethical principles in the conduct of research.

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

Sincerely,



Roberto Peccei
Vice Chancellor for Research

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

University of California, Los Angeles
CHANCELLOR'S ANIMAL RESEARCH COMMITTEE (ARC)

Notification of Investigators Regarding Sick or Injured Animals

This document delineates the responsibilities and obligations of DLAM and Investigators concerning sick or injured animals.

Upon finding a sick or injured animal, DLAM staff will mark the cage by placing a notification tag or post-it note next to the cage card and notifying the investigator's lab as soon as feasible thereafter. Depending on the urgency of the situation, this notification will be made via e-mail or telephone and will contain a summary description of the animal's condition as well as a recommendation for either treatment or euthanasia.

Upon receiving a sick or injured animal notification, **it is the responsibility of the Investigator** to do one of the following:

- 1) Start treatment prescribed by the veterinarian within the time frame stated on the email, and record, date & initial the Treatment Card, or
- 2) Euthanize the animal within the time frame stated on the email, or
- 3) Contact the attending veterinarian within the time frame stated on the email to discuss and agree upon an alternative course of action.

Please be aware that if none of the actions described in items # 1 – 3 above has occurred, the affected animal will be considered unattended and subject to euthanasia. An animal whose ongoing treatment is changed or discontinued by the research lab without the veterinarian's approval will also be considered unattended. **Failure of research personnel to carry out veterinary orders is considered a serious violation reportable to the NIH Office of Laboratory Animal Welfare.¹ It is unacceptable to simply fail to respond to such notification and expect DLAM staff to treat or euthanize the animal.**

DLAM veterinary staff members will make a reasonable effort² to communicate immediately with the research lab in cases where an animal is found moribund or, in the clinical judgment of the veterinarian, in a state of undue pain or distress. ~~If the~~ investigator cannot be reached, the animal may be euthanized in accordance with the *ARC Policy on Authority of the Attending Veterinarian*.

The Chancellor's Animal Research Committee (ARC) recognizes the importance of these animals to your research as well as our collective obligation to provide them with the best care possible. For humane and legal reasons, all animals must be treated or euthanized once a clinical problem has been reported.

¹ OLAW Notice #NOT-OD-05-034: *Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals* (available at <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-05-034.html>)

² DLAM will call the contact person designated on the cage card at the telephone number listed on the cage card.



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive - MSC 7982
Bethesda, Maryland 20892-7982
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
Facsimile: (301) 402-2803

November 28, 2007

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

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 November 12, 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). According to the information provided, OLAW understands that the Chancellor's Animal Research Committee (ARC) was notified on August 30, 2007 that mice had been administered a carcinogen, tamoxifen, in a location not approved for this purpose, at a dose and regimen not approved in the protocol and that one of the lab members had not completed the required training and was not listed on the protocol. This study is funded in part by the PHS.

Corrective actions consisted of a Biosafety Officer meeting with the PI to discuss moving the animals to an approved location and reminding the PI that the unapproved staff member was not permitted access to the animal facilities or allowed to handle animals until training was completed. The PI was also reminded of the requirement to follow all regulations concerning the use of biohazardous agents and carcinogens and that failure to adhere to the ARC approved protocol was considered a serious noncompliance.

OLAW understands that the protocol involved was PHS supported, and concurs that the incident warranted reporting. The actions taken by the UCLA ARC appear appropriate for the current incident, but this Office is concerned with the history of noncompliance concerning this PI and laboratory. This Office has recognized that it is sometimes necessary to appoint a more experienced and/or responsive PI or Co-PI to temporarily be responsible for animal work on protocols on which another PI has not demonstrated the ability to properly correct chronic noncompliance until such time that the original PI has completed remedial training or demonstrated to the Committee that noncompliances can be avoided. OLAW also requests that the ARC examine past issues concerning

this PI and laboratory to reconsider whether incidences were reportable to our Office. We especially draw the Committee's attention to the October 10, 2005 incident listed in your letter. If this and/or other incidents listed are considered reportable, please have appropriate personnel contact this Office. We appreciate being informed of this matter and request that you respond with your determinations by **January 11, 2008**.

Sincerely,

A handwritten signature in black ink, appearing to read "Brent C. Morse". The signature is fluid and cursive, with a long, sweeping underline that extends to the left.

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 L. Wadsworth, Associate Director – Animal Subjects Research

UCLA

UNIVERSITY OF CALIFORNIA,
LOS ANGELES

A3196-3V

ROBERTO PECCEI
Vice Chancellor for Research

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

November 12, 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: Report of Incident of Noncompliance
Animal Welfare Assurance A3196-01**

Dear Dr. Wolff:

I am writing to provide you with a report of an incident of noncompliance involving a non USDA-covered species (mice) used in a study conducted by a UCLA investigator. The study receives funding from various sources, including NIH grant #R24CA92865, NCI grant #441458/HWHW/33689, NCI grant #P50CA092131, NIH grant #1 RO1CA107166, NCI grant # CA119347-01, NCI grant #R01 CA121110-01A1, NEI grant #1PN2 EY018228, DOD grant #PC051307, DOD grant #PC 031130, and DOD grant #PC060326.

The Chancellor's Animal Research Committee (ARC) was notified on August 30, 2007 that mice used in the above referenced study may have been administered a carcinogen, tamoxifen, in a location which is not approved for this purpose. Additionally, according to notation on the cage cards, the mice appeared to have been administered daily injections of tamoxifen for at least two (2) weeks, at a dose of 2 mg. However, the ARC approved protocol states "Tamoxifen ... will be given intraperitoneally at 5mg/mice for 5 consecutive days." The ARC was also notified that one of the PI's lab members had access to her animals, but had not completed the required Division of Laboratory Animal Medicine (DLAM) training, and was not listed on the protocol.

NOV 20 '07 AM 9:57

In accordance with the ARC Policy, Investigating Allegations of Mistreatment or Other Noncompliance Issues¹, the Principal Investigator was contacted on September 4, 2007 and provided an opportunity to comment on the above noted incidents.

A UCLA Biosafety Officer met with the PI on Tuesday, September 4, 2007, to discuss procedures for transferring animals to the approved location. At that time, the Biosafety Officer reminded the PI that only those staff who have taken the appropriate Environmental Health & Safety training and DLAM barrier training required to work in the biocontainment facility would be allowed access to the room. At that time, the Biosafety Officer also informed the PI that the unapproved staff member was not permitted access to the animal facilities and could not handle animals until such time that the ARC grants approval.

The ARC reviewed the PI's response to the incidents during the convened meeting of September 7, 2007. Though the Committee appreciated the PI's willingness to address the violations pertaining to this protocol, the ARC expressed concern regarding her reaction to the violations, as well as her previous history of noncompliance, as noted below.

1. In response to the administration of a carcinogen (tamoxifen), in an unapproved location, the PI stated, "*we did perform tamoxifen injection in [the] biocontainment facility during the initial stage of our study. The medical fellows who were responsible for this study then reviewed medical literature to determine the actual biohazard potential of tamoxifen. Based on those published work and human clinical trials, they revised this procedure to consider the compounds tamoxifen and doxycycline as non-biohazardous.*"

The PI was reminded that UCLA is required to comply with all Federal, state and local, regulations pertaining to the use of biohazardous agents and carcinogens. Tamoxifen is listed as a known human carcinogen by the U.S. Department of Health and Human Service National Toxicology Program (January 31, 2005). As such, tamoxifen must be handled following the "NIH Guidelines for the Laboratory Use of Chemical Carcinogens" and meet the Cal/OSHA Chemical Hygiene Standard and, if applicable, other Cal/OSHA standard requirements. Conducting animal activities with carcinogens in a location not intended for the use of these chemicals is unacceptable, as personnel who handle animals, cages, or bedding may be exposed to these agents without adequate knowledge or personal protection.

2. In response to the unapproved change in dosing and dose schedule, the PI stated that the changes were made "to avoid potential side effects." Though the PI acknowledged that the modification "should have been included in the previously submitted amendment," the Committee reminded the PI that failure

¹ "In every investigation, the person(s) against whom the complaint has been raised shall be given notice of the concern and provided an opportunity to address the allegations in writing."

to adhere to the ARC approved protocol is considered a serious noncompliance reportable to the NIH/OLAW².

During the meeting of September 7, 2007, the ARC was reminded of prior instances in which the PI and her lab failed to adequately monitor animals or appropriately respond to health cases, despite numerous notifications and meetings with the DLAM veterinarians and ARC Chair William McBride. The following is a summary of these prior instances:

- On October 10, 2005, the PI was notified of several instances in which her lab failed to euthanize mice as requested in the DLAM Health Case and required by ARC Policy³. At that time, it was noted that the PI was personal. As such, this incident was not reported to the NIH/OLAW, and the PI was reminded to respond to future Health Cases in a timely fashion.
- On January 5, 2006, the DLAM veterinarians met with the PI to discuss the need for improved monitoring within her lab.
- On March 8, 2006 a second meeting was held between the PI and the DLAM veterinarians to discuss the recent failure to adequately monitor mice following irradiation, and discuss corrective actions to avoid animals dying on their own⁴.
- On April 28, 2006, the ARC was notified of continued deficiencies in your lab, despite the above referenced meetings and notifications. At that time, the PI were advised that future deficiencies may be reported to the NIH/OLAW. At that time, the PI provided her assurance that she would "reemphasize the requirement" to her lab staff that they comply with the ARC Policy.
- On July 19, 2006, ARC Chair William McBride contacted the PI to discuss a recent instance in which ten (10) mice had been found dead post-irradiation in less than one month. At that time, the PI commented that the deaths were the result of developmental related defects, and that she would continue to work with Clinical

² NIH Guidance Document, www.grants.nih.gov/grants/guide/notice-files/NOT-OD-05-034.html

³ "Upon receiving a sick or injured animal notification, it is the responsibility of the Investigator to... Start treatment prescribed by the veterinarian within the time frame stated on the email ... euthanize the animal within the time frame stated on the email, or contact the attending veterinarian within the time frame stated on the email to discuss and agree upon an alternative course of action. Failure of research personnel to carry out veterinary orders is considered a serious violation reportable to the [NIH/OLAW]." ARC Policy on Notification of Investigators Regarding Sick or Injured Animals www.oprs.ucla.edu/animal/help/manual/default.asp

⁴ "Legal, regulatory, and moral guidelines require that animal pain, distress, and suffering be minimized in any experiment. For these reasons, investigators are required to administer euthanasia in death endpoint experiments prior to the actual death of the animals unless experimental validity will be compromised." ARC Policy on Death as an Endpoint www.oprs.ucla.edu/animal/help/manual/default.asp

Veterinarian Gregory Lawson to identify the cause of the lethal phenotypes.

The members agreed that it was regrettable that these incidents were not reported as a serious incident prior to this most recent incident. However, in light of the lengthy history of deficiencies within the PI's lab, the Committee determined that the following corrective actions were required:

1. The PI was to contact Associate Director Kathy Wadsworth to schedule an ARC/DLAM Educational meeting with her and her lab to discuss ARC policies and DLAM procedures concerning her research. This was completed on September 27, 2007. In attendance were the PI, her lab staff, ARC Chair William McBride, Campus Veterinarian Marcelo Couto, Clinical Veterinarian Joanne Zahorsky-Reeves, and Ms. Wadsworth.
2. The PI was to contact the UCLA Biosafety Officer to schedule a retraining session in the proper handling and disposal methods of tamoxifen. This was completed on September 28, 2007.
3. The PI was to revise the current protocol to ensure that all contradictory statements regarding the safety of tamoxifen are revised and/or removed (e.g., "Based on published work and human clinical trials, no significant side effects have been reported." "carcasses will be disposed of per biohazard protocol given that tamoxifen is a mild carcinogen," "We have noted that injection of tamoxifen into pregnant mice...results in spontaneous abortion..."). This was completed as part of the PI's continuation application, which was approved October 18, 2007.
4. The PI was to review the current protocol to ensure that all dosing schedules are consistent with her current practice, and submit her application to the ARC for review and approval. This was completed as part of the PI's continuation application, which was approved October 18, 2007.

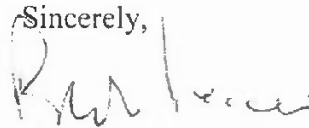
The Committee also reminded the PI that the University, investigators and their research staff, and the ARC share a collective responsibility for the ethical conduct of research at UCLA. This collaboration exists by upholding the highest ethical principles in the conduct of research. The Committee further reminded the PI that as Principal Investigator, she is responsible for upholding the federal, State and local policies and regulations governing the humane care and use of laboratory animals. As Principal Investigator, she is also responsible for ensuring that the research is conducted as described in the approved protocol, and that all personnel listed under her approved protocol understand all procedures described therein and perform their duties in

Axel V. Wolff, M.S., D.V.M.
November 12, 2007

Page 5

accordance with the aforementioned regulations and policies. The PI was further notified that that future incidents of noncompliance may result in suspension of your animal research.

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

Sincerely,


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

