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

January 9, 2008

Re: Animal Welfare Assurance
A3368-01 [OLAW Case 1K]

Dr. William S. Mellon
Associate Dean for Research Policy
University of Wisconsin-Madison
327 Bascom Hall – 500 Lincoln Drive
Madison, WI 53706-1380

Dear Dr. Mellon,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your January 4, 2008 letter reporting several instances of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Wisconsin- Madison, following up on an initial report for one of the incidents on July 10, 2007. According to the information provided, OLAW understands the following about the incidents and the corresponding corrective actions:

1) A dog died during a surgical procedure which included the conduct of an activity not described on the Institutional Animal Care and Use Committee (IACUC) approved protocol. Specifically, one kidney was to be removed and re-implanted however both kidneys were removed.

Corrective action: Future surgeries will have daily written plans which must be read and signed by each participant and then submitted to the manager. The Principal Investigator or designee must be present during surgery and all peri-operative records will be more closely monitored.

2) Two calves died after receiving too much lactic acid milk additive due to a feed mixing error.

Corrective action: Upon discovery the calves were treated but one died and the other was euthanized. The facility has stopped using the additive.

3) Four mice died after receiving an incorrectly diluted solution of cadmium sulfate.

Corrective action: The student responsible was reprimanded and retrained and the laboratory staff was counseled.

4) A sheep recovering from sedation aspirated rumen contents and died from pneumonia. The investigator responsible had left the animal before it was completely recovered.

Corrective action: The IACUC required the presence of qualified personnel to remain with an animal until recovery is complete. The laboratory will investigate other anesthetics with shorter recovery times and will contact the veterinarian when problems occur with anesthetic recoveries.

5) A whistleblower allegation about mishandling of mice was made to the IACUC but upon investigation, no basis to the allegation was substantiated.

6) Seventeen rats drowned due to a flood from a clogged pipe.
Corrective action: The pipe has been diverted from the animal room.

7) Five mice died from dehydration due to inability to reach water caused by a caging design defect.
Corrective action: The cage design was modified and animal care staff was retrained on health checks and contacting the veterinarian.

Based on its assessment of these explanations, OLAW understands that measures have been taken in each situation to correct and prevent recurrence of the problem. Please note that in accordance with issued guidance (enclosed) any matters falling under PHS Policy IV.F.3 are to be reported to this Office promptly, i.e., without delay. The protocols noted as having PHS funding must include the relevant grant number in the noncompliance report. We appreciate having been informed of these matters and find no cause for further action by this Office.

Sincerely,

Axel Wolff, M.S., D.V.M.
Director
Division of Compliance Oversight

cc: Eric Sandgren, Ph.D., IACUC Chair

Enclosure

THE UNIVERSITY of WISCONSIN MADISON

4 3368

January 4, 2008

Dr. Axel Wolff, MS, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
RKL1, Suite 360
6705 Rockledge Drive, MSC 7982
Bethesda, MD 20892-7892

Dear Dr. Wolff:

We are reporting several incidents that have occurred recently at the University of Wisconsin-Madison. One report is a follow-up to a telephone conversation that you had with Dr. Eric Sandgren.

In the first instance, a dog died during a kidney transplant surgery. The approved protocol provided for a kidney to be removed, held in solution, and then be reimplanted into the same animal. The surgeon (who is not the PI) deviated from protocol by removing both kidneys in sequence; it was during the second reimplantation that the animal died; the pathology report was inconclusive for cause of death. The investigator self-reported this deviation. The IACUC established several requirements for all future surgeries including: written daily plans for each surgery, which each staff member (including the surgeon) must read and sign off; the written daily plan must be submitted to the manager of the experimental surgery prior to each surgery; the PI or her designee must be present during all future surgeries; and increased monitoring of all animal health, surgical, postsurgical, and related records. This investigator has PHS funding.

In another incident, two calves died as the result of a feed mixing error by animal care staff. The animals were mistakenly fed too much of a lactic acid milk additive. The error was promptly noted and palliative treatment started immediately, but one calf had to be euthanized and the other died despite treatment. The dairy facility involved has discontinued all use of the additive and has no plans to reintroduce it. There is no PHS funding involved at this facility.

In another instance, four mice died from a dilution error involving cadmium sulfate solution. The graduate student involved immediately reported the incident to the PI, who self-reported the incident to the IACUC. The student was reprimanded and retrained, and the PI discussed with the entire laboratory the importance of checking solution strength. The IACUC felt the PI's response was appropriate. This PI is PHS funded.

JAN 7 '08 PM 3:27

Graduate School
Bascom Hall University of Wisconsin–Madison 500 Lincoln Drive Madison, Wisconsin 53706–1380

Deans' Office 608/262–1044 Fax: 608/262–5134
Graduate Admissions & Academic Services, Diversity Resources 608/262–2433, Fax: 608/265–9505
Accounting 608/262–5835 Fax: 608/262–5134
Human Resources 608/262–5802 Fax: 608/262–5235
Outreach & Graduate Student Professional Development 608/262–1044, Fax: 608/262–5134

A sheep was sedated for an imaging procedure, and was monitored until it was responsive, but not yet in sternal recumbency. At that point the scientist performing the monitoring was called away for a legitimate family emergency and the animal aspirated rumen contents and died of pneumonia. The IACUC required the laboratory to investigate different anesthesia methods that would reduce the length of recovery time, and that, regardless of anesthetic method, a trained member of the laboratory must remain with an animal until it can maintain sternal recumbency, hold up its head, and has an intact swallow reflex. In addition, the laboratory reviewed the procedures for contacting laboratory animal veterinarians in the case of poor or slow recovery. This PI does not have PHS funding.

The IACUC received a whistleblower report from a previous employee of a PI, regarding how the PI handled mice in the animal facility. An investigation was launched, including evaluation of animal well-being and records, observation of the PI and other staff handling mice, and an interview with the whistleblower, but the allegations could not be substantiated. This PI does not have PHS funding.

A flood caused by a clogged condensation drainpipe in the ceiling of a rat holding room caused the deaths of 17 adult rats overnight. Physical plant staff have rerouted the drainpipe.

Finally, five mice died when they could not reach water due to a design defect in new caging. The cage design has been refined, and animal care staff have been retrained on health checks and communication with veterinary staff.

If you have further questions or concerns, please contact Dr. Welter at 608/265-2695.

Sincerely,

Janet Welter, DVM, MPH, PhD
Diplomate ACLAM
Chief Campus Veterinarian

Eric Sandgren, DVM, PhD
Director, Animal Care and Use Program

William S. Mellon, PhD
Associate Dean for Research Policy

A3368-1A

Initial Report of Noncompliance

Date: 7/10/07 **Time:** 3:30

Name of Person reporting: Eric Sandgren
Telephone #:
Fax #:
Email:

Name of Institution: U of Wisconsin - Madison
Assurance number: A3368

Did incident involve PHS funded activity? ?
Funding component: _____
Was funding component contacted (if necessary): _____

What happened?
Dog study deviated from protocol
Death due to anesthetic

Species involved: DOG
Personnel involved:
Dates and times:
Animal deaths: 1

Projected plan and schedule for correction/prevention (if known): _____

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY
Case #_____

Full Assurance Agreement Printout

Assurance Number: A3368-01 **Prior Assurance Number:** A1457

Institution Name: University of Wisconsin - Madison

Institution Address: Madison, WI **Site:** 00

Dates:

Conditional Data Due:

Effective: 08/09/2004

Expiration: 07/31/2008

AR Reporting Cycle: 01/2008

AAALAC Status: 1

PHS Grant / Contract #:

Last Modified: 3/7/2007 **By:** jt

Chairman: Dr. Eric P. Sandgren **Degree:** Ph.D.

Title: Associate Professor

Address:
3450 Veterinary Medicine Bldg.-2015 Linden
Madison, WI 53706

Phone: (608) 263-8870 **Ext:**
Fax: (608) 263-9748

Email:

Official: Dr. William S. Mellon

Title: Associate Dean for Research Policy

Address:
327 Bascom Hall-500 Lincoln Drive
Madison. WI 53706-1380

Phone: (608) 262-1044 **Ext:**
Fax: (608) 262-5134

Email: wsmellon@bascom.wisc.edu

POC:

Title:

Address:

Phone: () **Ext:**
Fax: ()

Email:

Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals

Notice Number: NOT-OD-05-034

Key Dates

Release Date: February, 24, 2005

Issued by

Office of Laboratory Animal Welfare (OLAW), Office of Extramural Research
(http://grants.nih.gov/grants/olaw/olaw.htm)

This Notice provides guidance to Public Health Service (PHS) awardee institutions and Institutional Animal Care and Use Committees (IACUCs) on the prompt reporting requirements of the PHS Policy on Humane Care and Use of Laboratory Animals (Policy) (http://grants.nih.gov/grants/olaw/references/phspol.htm). This guidance is intended to assist IACUCs and Institutional Officials in determining what, when, and how situations should be reported under IV.F.3 of the Policy, and to promote greater uniformity in reporting. This Notice supersedes the January 12, 1994 Dear Colleague letter from the former Division of Animal Welfare, Office for Protection from Research Risks (now the Office of Laboratory Animal Welfare, or OLAW).

Background

PHS Policy, IV.F.3, requires that:

"The IACUC, through the Institutional Official, shall promptly provide OLAW with a full explanation of the circumstances and actions taken with respect to:

a) any serious or continuing noncompliance with this Policy;
b) any serious deviation from the provisions of the *Guide [for the Care and Use of Laboratory Animals]* ; or
c) any suspension of an activity by the IACUC."

IACUC suspensions of activities are cited at IV.C.6 and 7 of the Policy, and require a convened meeting of a quorum of the IACUC and the vote of a majority of the quorum present. The Institutional Official must review the reasons for suspension in consultation with the IACUC, take appropriate corrective action and report that action with full explanation to OLAW.

All institutions with Animal Welfare Assurances are required to comply with the provisions of IV.F.3. The Institutional Official signing the Assurance, in concert with the IACUC, is responsible for this reporting.

Reporting promptly to OLAW under IV.F.3 serves dual purposes. Foremost, it ensures that institutions deliberately address and correct situations that affect animal welfare, PHS-supported research, and compliance with the Policy. In addition, it enables OLAW to monitor the institution's animal care and use program oversight under the Policy, evaluate allegations of noncompliance, and assess the effectiveness of PHS policies and procedures.

The underlying foundation of the PHS Policy is one of institutional self-evaluation, self-monitoring and self-reporting. Public Law 99-158 (http://grants.nih.gov/grants/olaw/references/hrea1985.htm) requires that institutions be provided a reasonable opportunity to take corrective action before a grant or contract is suspended or terminated, and it is OLAW's role to assess whether the corrective actions reported by institutions under IV.F.3 are adequate. OLAW will assist the reporting institution in developing definitive corrective plans and schedules if necessary. Compliance actions affecting an award are rare because institutions are usually able to address incidents successfully and take appropriate actions to prevent recurrence.

Guidance on Prompt Reporting

A comprehensive list of definitive examples of reportable situations is impractical. Therefore, the examples below do

not cover all instances but demonstrate the threshold at which OLAW expects to receive a report. Institutions should use rational judgment in determining what situations meet the provisions of IV.F.3 and fall within the scope of the examples below, and consult with OLAW if in doubt. OLAW welcomes inquiries and discussion and will provide guidance with regard to specific situations. Situations that meet the provisions of IV.F.3 and are identified by external entities such as the United States Department of Agriculture or the Association for Assessment and Accreditation of Laboratory Animal Care International, or by individuals outside the IACUC or outside the institution, are not exempt from reporting under IV.F.3.

Examples of reportable situations:

- conditions that jeopardize the health or well-being of animals, including natural disasters, accidents, and mechanical failures, resulting in actual harm or death to animals;
- conduct of animal-related activities without appropriate IACUC review and approval;
- failure to adhere to IACUC-approved protocols;
- implementation of any significant change to IACUC-approved protocols without prior IACUC approval as required by IV.B.7.;
- conduct of animal-related activities beyond the expiration date established by the IACUC (note that a complete review under IV.C is required at least once every three years);
- conduct of official IACUC business requiring a quorum (full Committee review of an activity in accord with IV.C.2 or suspension in accord with IV.C.6) in the absence of a quorum;
- conduct of official IACUC business during a period of time that the Committee is improperly constituted;
- failure to correct deficiencies identified during the semiannual evaluation in a timely manner;
- chronic failure to provide space for animals in accordance with recommendations of the *Guide* unless the IACUC has approved a protocol-specific deviation from the *Guide* based on written scientific justification;
- participation in animal-related activities by individuals who have not been determined by the IACUC to be appropriately qualified and trained as required by IV.C.1.f;
- failure to monitor animals post-procedurally as necessary to ensure well-being (e.g., during recovery from anesthesia or during recuperation from invasive or debilitating procedures);
- failure to maintain appropriate animal-related records (e.g., identification, medical, husbandry);
- failure to ensure death of animals after euthanasia procedures (e.g., failed euthanasia with CO 2);
- failure of animal care and use personnel to carry out veterinary orders (e.g., treatments); or
- IACUC suspension or other institutional intervention that results in the temporary or permanent interruption of an activity due to noncompliance with the Policy, Animal Welfare Act, the *Guide* , or the institution's Animal Welfare Assurance.

OLAW recognizes that there may be levels of morbidity and mortality in virtually any animal-related activity, including those associated with the care and use of animals in research, testing, and teaching that are not the result of violations of either the Policy or the *Guide* . OLAW offers the following examples of situations which may *not* meet the threshold for reporting, based on consideration of the circumstances by the IACUC.

Examples of situations *not* normally required to be reported:

- death of animals that have reached the end of their natural life spans;
- death or failures of neonates to thrive when husbandry and veterinary medical oversight of dams and litters was appropriate;
- animal death or illness from spontaneous disease when appropriate quarantine, preventive 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; or
- infrequent incidents of drowning or near-drowning of rodents in cages when it is determined that the cause was water valves jammed with bedding (frequent problems of this nature, however, *must* be reported promptly along with corrective plans and schedules).

Time Frame for Reporting

Institutions should notify OLAW of matters falling under IV.F.3 promptly, i.e., without delay. Since IV.F.3 requires a full explanation of circumstances and actions taken and the time required to fully investigate and devise corrective actions may be lengthy, OLAW recommends that an authorized institutional representative provide a preliminary report to OLAW as soon as possible and follow-up with a thorough report once action has been taken. Preliminary reports may be in the form of a fax, email, or phone call. Reports should be submitted as situations occur, and not collected and submitted in groups or with the annual report to OLAW.

Information to Be Reported

Include as many of the following items of information as possible in the initial contact with OLAW. A follow-up report may address anything not known at the time of the initial report and should summarize the institution's corrective action. If a long term plan is necessary, describe the plan and include a reasonable schedule. This information will allow OLAW to assess the circumstances and actions taken to correct and prevent recurrence of the situation.

Information to be included:

- Animal Welfare Assurance number (http://grants.nih.gov/grants/olaw/assurance/300index.htm);
- relevant grant or contract number(s) if the situation is related to an activity directly supported by PHS;
- a full description of any potential or actual affect on PHS-supported activities if the situation is not directly supported by the PHS but is in a functional, programmatic, or physical area that could affect PHS-supported activities (e.g., inadequate program of veterinary care, training of technical/husbandry staff, or occupational health; inadequate sanitation due to malfunctioning cage washer; room temperature extremes due to HVAC failures);
- full explanation of the situation, including what happened, when and where, the species of animal(s) involved, and the category of individuals involved (e.g., principal or co-principal investigator, technician, animal caretaker, student, veterinarian, etc.);
- description of actions taken by the institution to address the situation; and
- description of short- or long-term corrective plans and implementation schedule(s).

Preliminary and final reports should be made to:

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
Phone: 301-594-2061
FAX: 301-402-2803
E-mail: olawdco@mail.nih.gov

Inquiries

For questions or further information, contact:

Director, Office of Laboratory Animal Welfare
Office of Extramural Research,
Office of the Director, National Institutes of Health
RKL 1, Suite 360
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(For express or hand-delivered mail use zip code 20817)
Telephone (301) 496-7163
olaw@od.nih.gov

Weekly TOC for this Announcement
NIH Funding Opportunities and Notices

Department of Health and Human Services

National Institutes of Health (NIH)
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