



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
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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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June 8, 2017

Re: Animal Welfare Assurance
#A3294-01 (OLAW Case 2E)
IACUC Case # 2017 - 05

Ernest D. Prentice, Ph.D.
Associate Vice Chancellor for
Academic Affairs & Regulatory Compliance
University of Nebraska Medical Center
987878 University Nebraska Medical Center
Omaha, NE 68198-7878

Dear Dr. Prentice,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your June 6, 2017 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Nebraska Medical Center. According to the information provided, OLAW understands that six rats died after receiving doses of anesthesia which were higher than what was required for the animals' body weight. This group of rats had been lighter than previous ones and the anesthetic dose had not been calculated according to body weight.

The corrective actions consisted of counseling and retraining the laboratory staff on protocol compliance, recalculating the anesthetic dose, and instructing the staff how to prepare the anesthetic cocktail. All anesthetics and catheters were replaced to avoid possible contamination. A heavier cohort of rats was subsequently ordered, the anesthetic dose was confirmed by the veterinarian, and the anesthesia was carried out without any adverse effects.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to prevent recurrence of this problem. OLAW concurs with the actions taken by the institution to comply with the PHS Policy.

Sincerely,

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

cc: IACUC Chair

June 6, 2017

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: IACUC Case #2017-05

Dear Dr. Wolff:

I am submitting this report in accordance with the requirements of the PHS Policy at IV.F.3. The IACUC has reviewed this incidence of the noncompliance and adverse event described in this report and categorized it as serious and, therefore, reportable to OLAW.

- 1. Animal Welfare Assurance Number:** A3294-01
- 2. Grant or Contract Number:** NA
- 3. Species:** Rats
- 4. Effects on Programmatic or Physical Areas:** NA
- 5. Explanation of the Situation:**
 - a. 6 rats with indwelling carotid artery catheters implanted by the vendor were anesthetized for protocol approved procedures of catheter maintenance, blood draws, and x-rays. The rats recovered from anesthesia, but the next morning 4 of the rats were found dead by husbandry staff. The following day one more rat was found dead. The sixth rat continued on the experiment as approved and was anesthetized for four consecutive days for procedures to be performed following smoke exposure, as described in the approved protocol. On day four the rat was anesthetized following smoke exposure and the rat died under anesthesia before the procedures could be performed.
 - b. The rats were smaller than the rats that were utilized for previous experiments on the same protocol. The anesthetic dose was not calculated according to bodyweight and the same amount was administered to all 6 rats. The calculated dose of anesthesia administered to the last surviving rat exceeded the approved dose.
 - c. The Comparative Medicine (CM) veterinarian was contacted and necropsies were performed and tissue samples were taken from 3 rats for histopathology to determine if the cause of death was a result of sepsis. The PI obtained chest x-rays from 2 rats that may have indicated existing pulmonary conditions. The results of the pathology were inconclusive, but did note lung injury in 2 out of 3 rats which may have been related to anesthesia complications. The report also indicated 1 rat had acute renal hemorrhage in the cortex which could be associated with acute bacteremia, but no bacteria were identified in the tissue.
 - d. The Protocol Assessment Liaison (PAL) and the CM veterinarian met with research personnel to discuss the incident and explore possible causes for the deaths. PAL provided education on protocol compliance. The protocol was reviewed and anesthetic doses were re-calculated and the lab was provided with CM's instructions for preparing the anesthetic cocktail. The PI replaced all anesthetics and catheter maintenance compounds to eliminate the possibility of contamination.
 - e. The next group of 6 rats was ordered at higher bodyweights and the CM veterinarian attended the next scheduled procedure. The veterinarian confirmed the correct concentration and dose

of anesthesia was administered to the rats. The rats recovered without incident, and there were no additional incidents reported for the remainder of the experiment.

6. Actions Taken by the IACUC:

- a. Following review of this incident by the IACUC subcommittee (IS) the recommendation was that this incident did constitute an adverse event and reportable noncompliance that jeopardized animal welfare. The subcommittee also determined that the corrective/preventative action plan was sufficient.
- b. On May 31, 2017 the IACUC voted to accept all recommendations of the IS as written.

7. Implementation Schedule:

- a. All corrective/preventative action has been implemented and completed.

If you have any questions or require any further information, please do not hesitate to contact me.

Sincerely,

Ernest D. Prentice, Ph.D.
Institutional Official
Associate Vice Chancellor for Academic Affairs
Regulatory Compliance

cc: Robert G. Bennett, Ph.D., IACUC Executive Chair
Robert S. Dixon, D.V.M., Director Comparative Medicine

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, June 08, 2017 8:01 AM
To: Secondary Individual
Subject: RE: Initial Report Adverse Event-Noncompliance UNMC/UNO IACUC Case #2017-05

Thank you for this report, Secondary Individual. We will send a response soon.

Axel Wolff

From: Secondary Individual [mailto:Secondary Individual@unmc.edu]
Sent: Wednesday, June 07, 2017 3:18 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Prentice, Ernest <edprenti@unmc.edu>; IACUCORA, UNMC <IACUCORA@unmc.edu>; Dixon, Robert S <rsdixon@unmc.edu>; Bennett, Robert G <rgbennet@unmc.edu>; Secondary Individual@unmc.edu>; Secondary Individual@unmc.edu>; Secondary Individual@unmc.edu>; Secondary Individual@unmc.edu>
Subject: Initial Report Adverse Event-Noncompliance UNMC/UNO IACUC Case #2017-05

June 7, 2017

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: IACUC Case #2017-05

Secondary Individual
Protocol Assessment Liaison (PAL)
Regulatory Affairs, IACUC
Phone: Phone Number
Cell: Phone Number

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