



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, Maryland 20892-6910
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 480-3387

April 28, 2020

Re: Animal Welfare Assurance
A3586-01 [OLAW Case 1R]

Dr. Toni M. Ganzel
Interim Institutional Official
Animal Care and Use Program
University of Louisville
323 E. Chestnut Street
Louisville, KY 40202

Dear Dr. Ganzel,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your April 21, 2020 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Louisville. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the University of Louisville Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to: failure to monitor animals post-procedure, use of anesthetic agent not approved on the animal protocol, and the conduct of euthanasia of animals that was not in compliance with the IACUC policy. The final report states on March 19, 2020 an RRF veterinarian contacted the investigator when 30 mice anesthetized with urethane were identified unresponsive in their cages after the laboratory failed to monitor the animals during recovery. The mice were monitored by RRF staff and recovered uneventfully with no health concerns identified. The Principal Investigator (PI) along with the RRF veterinarian reviewed the protocol and discovered urethane was not an approved agent and had been removed during the renewal process. The PI self-reported to the IACUC and had lab personnel review the protocol to prevent recurrence of the incident. Also, the report states the PI submitted an amendment to the IACUC to add urethane, which has since been approved. The IACUC also required the following corrective actions:

- Required all individuals in the lab responsible for anesthesia attend a training session with the RRF veterinarian on anesthesia monitoring, recovery and documentation.
- Required all lab members attend a training session with the IACUC Chair and Attending Veterinarian on the importance of adherence to the IACUC protocol and methods to prevent noncompliance.

The final report states on March 20, 2020 the IACUC received a self-report from a PI and formed a subcommittee to investigate the following event. The Committee determined on March 20th a PI euthanized ~100 mice on a protocol utilizing carbon dioxide in a manner not in compliance with the IACUC policy and AVMA Guidelines for the Euthanasia of Animals. It is stated that the investigator combined mice into a cage to hasten the euthanasia process and ignored compatibility and density requirements. As a result, during its meeting on April 16, 2020 the IACUC voted to suspend this protocol for 30 days.

The IACUC also implemented the following requirements:

- All approved project participants on the proposal must attend a training session with the IACUC Chair, Vice Chair, and Attending Veterinarian on the importance of adherence to IACUC policy and the approved Proposal.
- After the suspension is lifted, all euthanasia performed by the investigator must be supervised by an RRF veterinarian for the next six months.
- After the suspension is lifted, the next time euthanasia is performed by any other approved project participants it must be done so under the observation of an RRF veterinarian. Each member of the laboratory will be observed one time to ensure euthanasia is performed appropriately and in a humane and compliant manner.

It is understood that both incidents were partially supported by PHS funds. The report states the office of Grants and Contracts will assist the PIs in ensuring that any unauthorized costs initially billed to NIH grants will be covered by other sources. Based on its assessment of this explanation, OLAW understands that the University of Louisville has implemented appropriate measures to correct and prevent recurrences of these problems and is now compliant with provisions of the PHS Policy. We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,

Jacquelyn T. Tubbs -S

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Jacquelyn T. Tubbs -S
Date: 2020.04.28
11:49:26 -04'00'

Jacquelyn T. Tubbs, DVM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact

UNIVERSITY OF
LOUISVILLE

Toni M. Ganzel, M.D., MBA, FACS
Dean of the School of Medicine
Professor of Otolaryngology

April 21, 2020

Brent Morse, D.V.M.
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Room 3615
6705 Rockledge Drive
Bethesda, MD 20817-7982

Dear Dr. Morse:

This letter reports two events that the University of Louisville Institutional Animal Care and Use Committee (IACUC) deemed to meet the requirement for "deviation," as defined by our "Assurance of Compliance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals" (No. A3586-01).

1. On March 19, 2020, an RRF veterinarian contacted the investigator when 30 mice anesthetized with urethane were identified unresponsive in their cages after the laboratory failed to monitor the animals during recovery. RRF staff monitored the animals and checked on them the following day and no health concerns were identified. The investigator, in coordination with the RRF veterinarian, reviewed the IACUC *Proposal* 19603 and determined that urethane was not an approved agent and was inadvertently removed during the renewal process. The investigator self-reported the incident to the IACUC and had the laboratory review *Proposal* 19603 to prevent recurrences of this nature. The investigator also submitted a *Proposal* modification to the IACUC to add urethane; this has since been approved.

To protect animal welfare and ensure compliance, the IACUC has required that all individuals in the laboratory responsible for anesthesia attend a training session with an RRF veterinarian on anesthetic monitoring, recovery and documentation. The Committee has also required all members of the laboratory attend a training session with the IACUC Chair and Attending Veterinarian on the importance of adherence to the IACUC *Proposal* and methods to prevent noncompliance. *Note that records indicate that this study was at least partially supported by federal funds (R44DK117687, "IL-10 NanoCap for therapy of Familial Adenomatous Polyposis"; LC180086, "Overcoming anti-PD-1 resistance in lung cancer")*.

2. On March 20, 2020, the IACUC received a self-report from an investigator and formed a subcommittee to investigate the following event. The Committee determined that on March 20, 2020, the investigator euthanized approximately 100 mice under *Proposal* 19535 utilizing CO₂ in a manner not compliant with IACUC policy ("Euthanasia of Research Animals") and the *AVMA Guidelines for the Euthanasia of Animals*. Specifically, the investigator combined mice into a cage to hasten the euthanasia process and ignored compatibility and density requirements. Due to the gravity of the situation, during its meeting on April 16, 2020 the IACUC voted to suspend *Proposal* 19535 for thirty days.

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The IACUC has also implemented the following requirements:

1. All approved project participants on *Proposal* 19535 must attend a training session with the IACUC Chair, Vice Chair, and Attending Veterinarian on the importance of adherence to IACUC policy and the approved *Proposal*.
2. After the suspension is lifted, all euthanasia performed by the investigator must be supervised by an RRF veterinarian for the next six months.
3. After the suspension is lifted, the next time euthanasia is performed by any other approved project participants it must be done so under the observation of an RRF veterinarian. Each member of the laboratory will be observed one time to ensure euthanasia is performed appropriately and in a humane and compliant manner.

Note that records indicate that this study was at least partially supported by federal funds (2R01EY012354-17A1, "Isolation of Congenital Stationary Night Blindness Genes").

The IACUC has reminded the PIs that future incidents of noncompliance could result in limits on their laboratories' authorization to perform work with animal subjects. We believe that the IACUC's response to these incidents was appropriate and will serve to safeguard animal welfare and the institution's regulatory compliance. The UofL Office of Grants and Contracts will assist the PIs in ensuring that any unauthorized costs initially billed to NIH grants will be covered by other sources. Please note that a similar report has been filed with AAALAC International.

Sincerely,

(b) (6)

Toni M. Ganzel, M.D.
Institutional Official, Animal Care and Use Program

Cc: George M. Pantalos, Ph.D., IACUC Chair

Leslie C. Sherwood, D.V.M., Attending Veterinarian

Judy Bristow, Director, Sponsored Programs Administration

File

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, April 24, 2020 7:58 AM
To: Institutional Animal Care and Use Commit,Service Account
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Report of Noncompliance

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

Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: Institutional Animal Care and Use Commit,Service Account <iacuc@louisville.edu>
Sent: Thursday, April 23, 2020 2:54 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Ganzel,Toni Michelle <toni.ganzel@louisville.edu>; Sherwood,Leslie C <leslie.sherwood@louisville.edu>;
Pantalos,George <george.pantalos@louisville.edu>
Subject: Report of Noncompliance

Dear Dr. Morse,

Please find the attached report of noncompliance. Please let me know if you have any questions or require additional information.

Best Regards,

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(b) (6)