



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) 402-7065

April 11, 2019

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

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 March 29, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Louisville, following up on an initial report on February 27, 2019. According to the information provided, OLAW understands that mice were subjected to survival surgery although this had not been described in the approved protocol. This laboratory had been involved in previous noncompliance.

The corrective actions consisted of the Institutional Animal Care and Use Committee (IACUC) suspending the protocol. The Principal Investigator (PI) and staff were directed to take online retraining, the protocol was amended to add the surgery, the first several surgeries and post-operative care will be observed by a veterinarian and compliance specialist, and the laboratory will be subjected to enhanced post-approval monitoring by the IACUC. Upon completion of the corrective actions the suspension was lifted and the PI was warned about the consequences of future noncompliance. The NIH grant was not charged for any unauthorized animal activities.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the IACUC to comply with the PHS Policy. Please also directly inform the NIH funding component about the suspension. Thank you for keeping OLAW apprised on this matter.

Sincerely,

(b) (6)

Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare

cc: IACUC Chair

29 March 2019

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 is a final report regarding a noncompliance and IACUC proposal suspension by the University of Louisville Institutional Animal Care and Use Committee (IACUC) following a Principal Investigator's self-report of a "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). A preliminary report was submitted to OLAW on 3 March 2019.

On 6 February 2019, an investigator reported that mice were subjected to a survival surgery procedure that was not approved in the IACUC *Proposal*. The IACUC reviewed this report during its February meeting and voted to *suspend* the PI's active *Proposal* (18265) and to delay ongoing review of a modification to the *Proposal*. The IACUC formed a subcommittee to investigate the matter further. The subcommittee shared the results of their investigation and recommendations with the IACUC at its March meeting.

The subcommittee met with the laboratory during its investigation and held a training session. The subcommittee noted that the laboratory staff had recently reviewed the *Proposal* and the Principal Investigator was attentive to the matter. After discussing the subcommittee's report, and given the significance of conducting invasive research without IACUC approval and the investigator's past history of noncompliance, the IACUC decided to lift the suspension of the *Proposal* subject to the following conditions:

1. Members of the laboratory must complete the following CITI training modules before any surgical techniques may be performed. All members of the laboratory are required to complete the "Working with Mice in Research Settings" and "Post-Procedure Care of Mice and Rats in Research: Minimizing Pain and Distress" modules. In addition, the Principal Investigator and any personnel responsible for surgery must complete the "Aseptic Surgery" module in CITI.
2. The modification to the *Proposal* to add the surgical procedure will continue through the IACUC review process. Once approved, to ensure that adequate training has been provided the first three surgical procedures performed will be observed by an RRF veterinarian and the IACUC Animal

Compliance Specialist. Both will follow-up after the surgeries to train laboratory staff and ensure that post-procedural care and recordkeeping are appropriate and complete.

3. The laboratory will be subject to at least two unannounced visits by the IACUC over the next six months to ensure that they remain in compliance.

Note that records indicate this study was at least partially supported by federal funds (SUH3TR000875-05, "Fruit exosome-like particles for therapeutic delivery of extracellular miRNAs"; 1R01AT008617-01A1, "Plant exosomes non-coding RNA-mediated anti-inflammatory mechanisms").

The IACUC has reminded the PI that future incidents of non-compliance could result in limits on the laboratory's authorization to perform work with animal subjects. We believe that the IACUC's response to the incident was appropriate and will serve to safeguard animal welfare and the institution's regulatory compliance. Please note that similar reports have been filed with both USDA and AAALAC International.

Sincerely,

(b) (6)

Toni M. Ganzel, M.D.

Interim Institutional Official, Animal Care and Use Program

cc: George Pantalos, Ph.D., IACUC Chair

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

(b) (6)

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, April 10, 2019 12:26 PM
To: Institutional Animal Care and Use Commit,Service Account; OLAW Division of Compliance Oversight (NIH/OD)
Cc: Sherwood,Leslie C
Subject: RE: Final Report of Noncompliance and Proposal Suspension

Thank you for providing this report. We will send an official response soon.

Best regards, Brent Morse

Brent C. Morse, DVM, DACLAM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

Please note that this message and any of its attachments are intended for the named recipient(s) only and may contain confidential, protected or privileged information that should not be distributed to unauthorized individuals. If you have received this message in error, please contact the sender.

From: Institutional Animal Care and Use Commit,Service Account [mailto:iacuc@louisville.edu]
Sent: Tuesday, April 02, 2019 9:59 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Sherwood,Leslie C <leslie.sherwood@louisville.edu>
Subject: Final Report of Noncompliance and Proposal Suspension

Dear Dr. Morse,

I am submitting the following on behalf of Dr. Leslie Sherwood. Please find a letter attached detailing the final report of noncompliance following the preliminary report sent in March. Please let me know if you have any questions or require additional information.

Best Regards,

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UNIVERSITY OF
LOUISVILLE

27 February 2019

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 a suspension by the University of Louisville Institutional Animal Care and Use Committee (IACUC) following a Principal Investigator's self-report of a "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).

On 6 February 2019, an investigator reported that mice were subjected to a survival surgery procedure that was not approved in the IACUC Proposal. The IACUC reviewed this report during its February meeting and has formed a subcommittee to investigate the matter further. Of particular concern to the Committee was the consistency of this noncompliance with prior noncompliant behavior in 2015. Given the significance of conducting invasive research without IACUC approval and the investigator's past history of noncompliance, the Committee voted to suspend the PI's active Proposal (18265) and to delay ongoing review of a modification to the Proposal. Note that records indicate that this study was at least partially supported by federal funds (5UH3TR000875-05, "Fruit exosome-like particles for therapeutic delivery of extracellular miRNAs"; 1R01AT008617-01A1, "Plant exosomes non-coding RNA-mediated anti-inflammatory mechanisms").

We believe that the IACUC's response to the incidents was appropriate. A follow-up report will be sent to OLAW after the IACUC subcommittee completes its investigation detailing the findings and the IACUC's course of action. The UofL Office of Grants and Contracts will assist the PI in ensuring that any unauthorized costs initially billed to NIH grants will be covered by other sources. Please note that similar reports have been filed with both USDA and AAALAC International.

Sincerely,

(b) (6)

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

Cc: George M. Pantalos, Ph.D., IACUC Chair
Leslie C. Sherwood, D.V.M., Attending Veterinarian

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Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, March 5, 2019 6:57 AM
To: 'Sherwood,Leslie C'
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Preliminary report of Noncompliance and Proposal Suspension

Thank you for this preliminary report, Dr. Sherwood. We will open a new case file and look forward to receiving the final report from the IO after the IACUC has completed its investigation.

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

From: Sherwood,Leslie C <leslie.sherwood@louisville.edu>
Sent: Monday, March 4, 2019 3:03 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Institutional Animal Care and Use Commit,Service Account <iacuc@louisville.edu>
Subject: Preliminary report of Noncompliance and Proposal Suspension

Dear Dr. Morse,

Please find a letter attached detailing a preliminary report of noncompliance that our IACUC is currently investigating. Please let me know if you have any questions or require additional information. I will send a final report as soon as it is available.

Best,

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**UNIVERSITY OF
LOUISVILLE.**