



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, MD 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

March 1, 2022

Re: Animal Welfare Assurance
A3914-01 [OLAW Case 1S]

Dr. Timothy Denning
Vice President for Research and Economic Development
Georgia State University
100 Auburn Ave NE, (b) (4)
Atlanta, GA 30303

Dear Dr. Denning,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your February 11, 2022 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Georgia State University. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the Georgia State University Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to: failure to adhere to the IACUC-approved protocol. The final report states on December 8, 2021, the Attending Veterinarian (AV) performed a clinical check on one of five rats that underwent implantation of osmotic mini pumps. A review of surgical records indicated buprenorphine had been administered to the animal, but it was unclear if buprenorphine sustained release (SR) had been administered to the rat. Protocol review revealed the approved analgesic was carprofen and not buprenorphine. It was also determined that the dosage of buprenorphine administered to the animal was the dosage for mice and not rats. Further review of past surgical records revealed a total of 14 rats were given the unapproved analgesic and at the incorrect dosage. In response to the findings, the lab halted the surgical procedure (at the advice of the AV) until the IACUC could review the matter.

The matter was discussed during the December 17, 2021 meeting of the IACUC. The committee determined the incident constituted a continuous noncompliance. The IACUC provided additional requirements the lab must implement which included the following:

- Surgical procedures must be observed/monitored by veterinary staff until lab personnel are deemed sufficiently trained to perform surgeries without oversight.
- Pertaining to all the investigator's IACUC protocols, all lab members must write out the specific protocol procedures for all procedures that require analgesia. Individuals must document/confirm and sign off that the procedures are compliant with the protocol and have been read prior to starting the procedure. Documents will be reviewed by veterinary staff. These documents must be kept with the DAR surgical records.
- Frequency of post-approval monitoring visits to the lab will increase.

It is noted that this research is not supported by PHS funding. Based on its assessment of this explanation, OLAW understands that the Georgia State University has implemented appropriate measures to correct and prevent recurrences of these problems and is now compliant with provisions of the PHS Policy.

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March 1, 2022
OLAW Case A3914-1S

We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,

Jacquelyn T. Tubbs -S

Digitally signed by
Jacquelyn T. Tubbs -S
Date: 2022.03.01
15:46:41 -05'00'

Jacquelyn Tubbs, DVM, DACLAM
Senior Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact

Mailing Address:
P.O. Box 3999
Atlanta, GA 30302-3999

In Person:
Centennial Hall, Suite 532
100 Auburn Ave NE
Atlanta, GA 30303

Phone: 404-413-3517
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Web: www.gsu.edu/research



February 11, 2022

To: Brent Morse, DVM
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: Non-Compliance of IACUC Protocol A19054
PI: Ming-Hui Zou PhD
Entitled "Endothelial cell dysfunction in pulmonary hypertension"
Funding Source: Non-PHS funded

The Georgia State University IACUC (PHS Assurance Number D16-00527 (A3914-01)) investigated a non-compliance issue that was brought to their attention by the Attending Veterinarian (AV). On 12/8/2021, the AV performed a clinical check on one of five rats that had an osmotic mini pump implanted. When he examined the rat, the AV reviewed the surgical record for this animal. The surgical record indicated that buprenorphine was administered but it was unclear if the agent was buprenorphine SR. Upon review of the IACUC protocol, the AV noted carprofen was the approved analgesic on the relevant protocol. The dosage administered to the rats, 0.5 mg/kg, is one approved for mice, not rats; the accurate dosage for rats is 1-2 mg/kg. Consequently, all five rats were provided the incorrect analgesic and dosage. Upon further review of past surgical records, surgeries were performed on 11/22/21 (3 rats), 11/29/21 (3 rats), and on 12/1/21 (3 rats) during which all 14 rats were provided with the wrong analgesic and inadequate dosage. With assistance from veterinarian staff, carprofen was then administered to the animals. At the advice of the AV, the lab ceased the surgical procedure until the IACUC could review of the matter.

The IACUC discussed this information during the December 17, 2021, IACUC meeting. The IACUC determined this incident constituted a continuous noncompliance event because the lab members:

- Failed to follow the relevant IACUC protocol on multiple occasions.
- Failed to provide the proper analgesic and correct dosage to animals.

The IACUC accepted the PI's current measure to cease the surgical procedure until IACUC review and provided additional requirements the lab must implement:

- Surgical procedures must be observed/monitored by veterinary staff until lab personnel are deemed sufficiently trained to perform surgeries without oversight.
- Across all of Dr. Zou's IACUC protocols, all lab members must write out the specific protocol

procedures for all procedures that require analgesia. Individuals must document/confirm and sign off that the procedures are compliant with the protocol and have been read prior to starting the procedure. Documents will be reviewed by veterinary staff. These documents must be kept with the DAR surgical records.

- Frequency of post-approval monitoring visits to Zou lab will increase.

The investigator is aware that further violations of IACUC protocols or failure to implement corrective actions as set forth by the IACUC may result in additional sanctions, including permanent suspension of all IACUC protocols.

Please note that IACUC protocol A19054 is institutionally funded. This incident meets the criteria for reporting to the Office of Laboratory Animal Welfare (OLAW), under the directive of OLAW Notice #: NOT-OD-05-034, "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.
- Failure to adhere to IACUC-approved protocols.

If you have any questions concerning these issues, please feel free to contact me.

Sincerely,

(b) (6)

Timothy L. Denning, Ph.D.
Vice President for Research and Economic Development
Distinguished University Professor

Cc: IACUC file
IACUC Chair
Attending Veterinarian
AAALAC

Tubbs, Jai (NIH/OD) [E]

From: Institutional Animal Care and Use Program <iacuc@gsu.edu>
Sent: Wednesday, February 23, 2022 2:48 PM
To: OLAW Division of Compliance Oversight (NIH/OD); Tubbs, Jai (NIH/OD) [E]; 'accredit@aaalac.org'
Cc: Timothy Luke Denning; (b) (6)
Subject: (b) (6) Institutional Animal Care and Use Program [EXTERNAL] OLAW Notification GSU (Assurance #A3914-01)- IACUC Protocol-NC- Final Report
Attachments: OLAW Letter - Noncompliance Protocol A 19054 Final Letter - Final.TLD.pdf
Follow Up Flag: Follow up
Flag Status: Flagged

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Good Afternoon,
Please see the attached final report from Georgia State University. Please contact GSU's Office for questions or concerns.

Sincerely,

(b) (6)