



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

September 29, 2021

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

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 June 3, 2021 final letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Georgia State University. According to the information provided, OLAW understands that Division of Animal Resources (DAR) staff found a rat alive in the carcass freezer after it was supposedly euthanized by a research associate approximately two hours prior to being found. Upon investigation, it was found that rats were exposed to CO₂ for 5-7 minutes according to standard protocol and breathing cessation was verified followed by secondary cervical dislocation using 14.5cm metal scissors pressed against the neck. Cervical dislocation as a secondary method of euthanasia following CO₂ administration is approved on the protocol. The research associate was under the impression cervical dislocation procedures were completed successfully when the animals were placed in the carcass freezer. The rats were 550-600grams which is larger than typically used by the research associate. The research associate indicated this technique was used successfully for over 10 years without issue however he was aware cervical dislocation was not recommended as a secondary procedure is the rat weight exceeded 200grams. The study was PHS funded.

As a corrective measure, the PI reviewed approved secondary euthanasia procedures with laboratory staff and informed staff that cervical dislocation will no longer be used as a secondary method of euthanasia on rats of any size. The Attending Veterinarian provided training to all laboratory members on bilateral thoracotomy as an alternative secondary method. The IACUC Policy on Carbon Dioxide Euthanasia will be revised to state that cervical dislocation must not be used as a secondary method for rats exceeding 200grams. The PI has been notified that further violations could result in additional sanctions including permanent suspension of IACUC protocols as well as other research activities involving animals.

OLAW appreciates the prompt consideration of this matter by Georgia State University which is consistent with the philosophy of institutional self-regulation. OLAW expects continuing post-approval monitoring to prevent recurrence of this non-compliance and potential associated animal welfare concerns. Based on the information provided, OLAW is satisfied that appropriate steps have been taken to investigate this incident and to attempt to prevent recurrence.

We appreciate being informed of this matter and please contact us with any further questions or concerns.

Sincerely,

(b) (6)

Nicole Lukovsky-Akhsanov, DVM, MPH, DACLAM
Division of Compliance Oversight
Office of Laboratory Animal Welfare

CC: IACUC contact

VICE PRESIDENT FOR RESEARCH & ECONOMIC DEVELOPMENT
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June 03, 2021

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 A21007
PI: Javier Stern

(b) (6)

Entitled "Altered CNS Intercellular Signaling Mechanisms in Cardiometabolic Disease"
Funding Source: **NIH #RO1HL090948**, "Altered CNS intercellular mechanisms in cardiovascular disease; **NIH #RO1NS094640**, "Dendritic release of neuropeptides: role in bodily homeostasis; **NIH #1 F32 HL158172-01**, "Activity-dependent organelle calcium dynamics and their impact on firing activity in vasopressin neurons during heart failure"

The Georgia State University IACUC (PHS Assurance Number D16-00527 (A3914-01)) investigated a non-compliance issue that was brought to the committee's attention by the principal investigator, Dr. Javier Stern, on May 21, 2021. The Attending Veterinarian informed the PI that DAR staff had found a supposedly euthanized rat alive in the carcass freezer in the facility. This animal belonged to a group of four rats which had been euthanized by carbon dioxide by a member of Dr. Stern's laboratory, (b) (6) approximately two hours prior to this rat being found alive in the carcass freezer. The PI immediately contacted and met with (b) (6) to obtain a detailed account of the procedures (b) (6) performed.

(b) (6) stated that at approximately 12pm on May 20, 2021, (b) (6) performed routine euthanasia procedures on four rats that would no longer be used in any of the lab's ongoing experiments. (b) (6) exposed the rats for 5-7 minutes to CO2 according to standard protocol and verified that breathing had ceased. Next, (b) (6) performed the secondary procedure routinely used, cervical dislocation, using 14.5 cm metal scissors pressed against the neck. It was identified that these rats were significantly larger (body weight approximately 550-600 g) than those typically used by (b) (6) for (b) (6) experiments. (b) (6) indicated that (b) (6) was aware that cervical dislocation is not recommended as a secondary procedure if rat body weight exceeds 200g,

but (b) (6) indicated that (b) (6) has utilized this technique for over 10 years with no issues. (b) (6) was under the impression that (b) (6) had successfully completed the cervical dislocation procedure when (b) (6) placed the animals in the designated carcass freezer.

I. Findings Presented to the IACUC at the May 28, 2021 meeting:

- (b) (6) performed cervical dislocation as a secondary method of euthanasia following CO2 administration on rats as per the approved protocol A21007. The rats on which the euthanasia was conducted were much larger than the rats this individual normally euthanizes.
- (b) (6) was aware that cervical dislocation is not recommended for rats over 200 g when (b) (6) performed the euthanasia procedure in rats weighing between 550g-600g. However, (b) (6) indicated that (b) (6) had performed the procedure many times and never encountered issues.
- The GSU IACUC Policy on Carbon Dioxide Euthanasia addresses secondary methods of euthanasia to include cervical dislocation but does not specifically address the stipulation that cervical dislocation is not an appropriate secondary method of euthanasia for rats weighing over 200 grams. The committee decided the policy should be revised to specifically state this.
- (b) (6) reviewed the steps (b) (6) followed and appreciated that (b) (6) was mistaken when concluding that the cervical dislocation procedures performed on these animals were successful.

II. Noncompliance Associated with IACUC Protocol A21007:

- Application of an unapproved secondary euthanasia procedure and failure to properly validate that animals were deceased.

III. Sanctions and Corrective Actions

- The PI reviewed with all members of the laboratory the approved secondary euthanasia procedures.
- The PI has informed laboratory members that they are to no longer to use cervical dislocation as a secondary method of euthanasia on rats of any size. Rather, they can continue to use decapitation via a guillotine as the follow-up method of euthanasia after CO2 administration, regardless of the body weight of the animal.
- In addition, the Attending Veterinarian provided training to all laboratory members on bilateral thoracotomy as an alternative secondary method of euthanasia.
- The IACUC will revise the GSU Carbon Dioxide Euthanasia Policy to state that cervical dislocation must not be used as a secondary method on rats with a body weight exceeding 200g.

Georgia State University is reporting this non-compliance/adverse events to OLAW under the directive of OLAW Notice #: NOT-OD-05-034, "Examples of reportable situations:

- failure to ensure death of animals after euthanasia procedures (e.g., failed euthanasia with CO₂)."

Georgia State University is fully aware of the seriousness of this IACUC protocol compliance violation. The PI has been notified that further violations of IACUC protocols could result in additional sanctions, including permanent suspension of IACUC protocols as well as other research activities involving animals. If you have any questions concerning this incident and response measures taken, 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

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, June 25, 2021 7:08 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: OLAW Final Notification GSU (Assurance #A3914-01)- IACUC Protocol-Noncompliance

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

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

From: (b) (6)
Sent: Wednesday, June 23, 2021 12:45 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; jaquelyn.tubbs@nih.gov
Cc: (b) (6)
Subject: OLAW Final Notification GSU (Assurance #A3914-01)- IACUC Protocol-Noncompliance

Good Afternoon,

Please see the attached final report from Georgia State University.

(b) (6)

