DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

Office of Laboratory Animal Welfare
Bethesda, Maryland 20892

Telephone: (301) 496-7163
Home Page: https://olaw.nih.gov

January 27, 2026

Re: Animal Welfare Assurance
A3172-01 [OLAW Case M]

Kenneth Fridley, Ph.D., F.ASCE
Vice President for Research & Economic Development
Old Dominion University
4111 Monarch Way, (b) (4)
Norfolk, VA 23508

Dear Dr. Fridley,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your December 5, 2025, letter reporting an adverse event and an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Old Dominion University following up on an initial November 14, 2025, notification by telephone. It is noted the research project is not supported by PHS funding.

According to the information provided, this Office understands that the Old Dominion University Institutional Animal Care and Use Committee (IACUC) determined that instances of noncompliance occurred with respect to an unapproved change in analgesic and an adverse event regarding failure of animals to recover from anesthesia. The final report states on October 6, 2025, an approved survival surgical procedure was conducted on mice by a highly trained research team. The procedure required surgical anesthesia with a 40-50min recovery period in an oxygen chamber maintained on a heating pad. It is stated the first group of 10 mice were anesthetized (20 mice in total were planned for the day), and one animal displayed altered respiratory patterns and was moved to the oxygen chamber for recovery prior to any surgery. The animal died within 10min of being placed in the recovery chamber. It is stated 5 additional mice had prolonged recovery from anesthesia following the surgical procedure. Ultimately, a total of 6 mice did not recover from anesthesia, despite attempts to resuscitate the animals. It is noted that the remaining animals were closely monitored but their recovery was not documented.

Per the report, the research team used a newly prepared anesthetic mixture following the death of the first animal. It is stated that 10 additional mice were anesthetized, underwent the surgery, but were not treated experimentally. Two of the animals in this group did not recover from anesthesia and the remaining animals were returned to their cages. However, the next day 3 additional mice were found dead. It is understood that the research team submitted an adverse event as per the IACUC guidelines, and that the committee requested the team cease all animal activity. It is stated the remaining animals in the two cohort sets were assessed and no additional complications were identified.

The IACUC conducted an investigation into the matter. In summary, the following findings resulted from the committee's investigation and review of the events:

- Necropsy results on the 11 mice were inconclusive and did not reveal a definitive cause of the mortality. However, it was noted that the findings were consistent with anesthesia-induced hypoxia.
- The Attending Veterinarian (AV) evaluated the anesthetic procedure and dosage and determined they adhered to the protocol; however, proper records were not maintained by the research team.
- No issues were identified with the equipment used by the research team.

In response to the incident, the following corrective measures were implemented by the IACUC (in summary):

- Submission of an amendment to standardize the anesthetic cocktail preparation to a 10ml batch to improve dosing precision and enhance the safety margin.
- Addition of atipamezole to the approved anesthetic protocol for use on an as-needed basis, to counteract residual xylazine effects and ensure safer recovery, post-procedure.
- The research team will receive mandatory training sessions regarding aseptic technique, drug preparation practices, pre-operative preparations, and post-operative care.
- The research team must attend a Project Implementation Meeting conducted by the AV and the Research Compliance Coordinator to review the protocol and recordkeeping ensuring compliance with the IACUC-approved protocol.
- Reinforcement of proper aseptic techniques during anesthetic preparation and surgical procedures.
- Implementation of mandatory, hands-on retraining in anesthesia, surgical technique, and recordkeeping for all personnel involved in animal procedures.
- Unannounced veterinary and additional post-approval monitoring inspections will be conducted during procedures and in lab spaces until consistent compliance is demonstrated, for a period of at least one year.

The IACUC's investigation revealed an unapproved change in an analgesic by the lab. It is stated that Buprenorphine-XR was administered instead of the protocol-approved buprenorphine (0.05 mg/kg) without a prior IACUC amendment or VVC approval. It is also stated that documentation of the analgesic dosing and administration was not maintained. Per the report, this analgesic was not used in experiments related to this adverse event. It is understood that since the conclusion of the IACUC's investigation, the research team and the IACUC have implemented corrective and preventative measures to prevent future recurrence of a similar incident.

Based on the information provided, the Office of Laboratory Animal Welfare (OLAW) is satisfied that appropriate actions have been taken to investigate, correct, and prevent recurrence of the noncompliance.

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: 2026.01.27 13:36:50 -05'00'

Jacquelyn Tubbs, DVM, DACLAM
Acting Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact

A3172-M

OLD DOMINION UNIVERSITY
Division of Research and Economic Development

Office of Laboratory Animal Welfare
Division of Compliance Oversight

December 5, 2025

To Whom It May Concern,

On behalf of the Institutional Animal Care and Use Committee (IACUC) at Old Dominion University [D16-00110 (A3172-01)], this letter is intended to summarize a reportable adverse event involving the failure of animals to recover from anesthesia during an approved experimental procedure, and to outline the actions taken to date. A preliminary report has already been submitted to your office.

Summary of the Event

On October 6, 2025, a planned non-terminal surgical procedure was conducted under IACUC-approved Protocol # 24-001, involving (b) (6) mice. The procedure was carried out by a highly trained research team, including a PhD/DVM and a PhD/MD, with 5 and 4 years of experience in performing surgeries on rodents, corresponding to 400+ and 300+ surgeries, respectively. The procedure required surgical anesthesia and typically took 5 to 7 minutes per animal, followed by 40 to 50 minute recovery period inside an oxygen chamber while on a heating pad. Return to the holding cage usually occurred within 150 minutes from the start of the procedure. The investigators planned to use 20 mice on the day of the experiment.

The first group of 10 mice were anesthetized. After some of the animals had undergone the surgical procedure and experimental treatment, one mouse exhibited altered respiratory patterns and was immediately moved to the oxygen chamber for recovery before any surgery was performed. The mouse died within 10 minutes of being placed in the recovery chamber. Five additional mice were taking longer than usual to recover from anesthesia after the surgical procedure. Within an hour initiating the procedures, a total of six mice failed to recover from anesthesia, despite attempts of CPR and oxygen supplementation. Recovery of the remaining animals was closely monitored but not recorded. The vivarium staff were notified.

After the first mouse died, the research team decided to proceed with the experiment using a newly prepared anesthetic mixture, suspecting a compromised drug cocktail as the likely cause of animal mortality. Ten additional mice were anesthetized and underwent the surgical procedure but were not treated experimentally. Two of these ten mice also failed to recover from anesthesia and died. The remaining mice, after recovery, were returned to their cages. The following morning, three additional mice were found dead; one from the original set of mice and two from the second set.

Division of Research and Economic Development
4111 Monarch Way, (b) (4), Norfolk, VA 23508 ▪ Phone (b) (6) ▪ Fax: (b) (6)
www.odu.edu/research

Immediate Actions Taken

- The research team submitted an adverse event report at the end of the day in accordance with ODU IACUC Guidelines on prompt reporting of adverse events.
- The IACUC requested that all animal research activity on any of the protocols associated with the three researchers involved (the PI, PhD/DVM, PhD/MD) stop immediately until the event could be investigated. The team stopped all work.
- The attending veterinarian performed necropsies on the 11 mice as part of a preliminary assessment within 24 hours of the incident.
- The remaining nine animals in the two cohort sets were evaluated and no additional complications were observed.

IACUC Review and Investigation

The IACUC has conducted a thorough review of the incident, including:

- The adverse event sub-committee convened to conduct a preliminary review of the incident based on the AV's report.
    - The necropsy results were inconclusive and did not identify a definitive cause of mortality. Anesthesia issues were considered but because of the research group's extensive experience with both the anesthesia and surgical procedures, other contributing factors could not be ruled out.
- The IACUC requested that the Principal Investigator (PI) provide a detailed overview of the event, detailing the timeline, personnel involved, anesthetic regimen, and procedural conditions.
- The AV assessed the anesthetic preparation procedure and dosage and found them to be as described in the protocol but noted that appropriate drug administration records were not maintained by the research team.
- The animal facility staff performed a thorough examination of equipment to determine if they were functioning properly and reviewed calibration records; no issues were found with the equipment used during the procedures.
- Verification that the research team was within the scope of the approved IACUC protocol and standard operating procedures were reviewed by the full committee during the monthly IACUC meeting held on October 23, 2025. The PI and the entire research team associated with the event were present at the IACUC meeting to address questions from the committee.

The committee noted that the exact cause of death could not be accurately determined, due to inadequate records, although the outcomes of the necropsy are consistent with anesthesia-induced hypoxia.

Furthermore, the committee and the research team proposed that the anesthetic mix most likely contributed to the animal mortality. There was no evidence of willful neglect. The research team notified the committee within the time frame specified by the ODU IACUC Guidelines and was open to implementation of corrective measures suggested by the committee.

Corrective and Preventive Actions, as well as Institutional Commitment and Oversight
To prevent a reoccurrence, the IACUC is requiring the following corrective actions be taken by the research team:

1. Submit an amendment on IRBNet specifying the following:
    a. Standardize anesthetic cocktail preparation to a 10 mL batch to improve dosing precision and enhance the safety margin, as the previous 2 mL preparation increased the risk of measurement error.
    b. Addition of atipamezole (0.5–1 mg/kg IP) to the approved anesthetic protocol for use on an as-needed basis, to counteract residual xylazine effects and ensure safer recovery, post-procedure. The amendment should indicate that the reversal agent can be administered if recovery exceeds 120 minutes or if animals exhibit prolonged sedation, shallow respiration, or delayed reflexes.
    c. **OPTIONAL:** A request for a pilot study, at the PI's discretion, that may be conducted with veterinary assistance using a small cohort to assess anesthetic depth, recovery time, and tolerance to the revised protocol.
2. The research team must receive mandatory training sessions conducted by the attending veterinarian in regard to:
    a. Aseptic technique and drug preparation practices, emphasizing dosing accuracy.
    b. Peri-operative preparations and post-operative care, including record keeping. Monitoring procedures listed in the protocol must be followed and information from the monitoring recorded.
3. Prior to resuming animal work, the research team must attend a Project Implementation Meeting (PIM) conducted by the attending veterinarian and the Research Compliance Coordinator to review the protocol and record keeping ensuring compliance with the IACUC-approved protocol, as well as ODU IACUC Guidelines.
4. Any changes to a protocol, such as a change in analgesia, must be submitted as an amendment and approved by either the attending veterinarian through the Veterinary Verification and Consultation (VVC) program, Designated Member Review (DMR) or Full Committee Review (FCR), prior to implementation to ensure standard of care is being maintained.
5. Ensure complete peri- and post-operative recordkeeping, including anesthetic monitoring, surgical details, and recovery observations, to be reviewed and signed by veterinary staff. An IACUC-approved data recording sheet **must** be used for all procedures involving anesthesia/analgesics and/or surgical procedures.
6. Reinforce proper aseptic techniques during anesthetic preparation and surgical procedures to maintain sterility standards.
7. Implement mandatory, hands-on retraining in anesthesia, surgical technique, and recordkeeping for all personnel involved in animal procedures.
8. Following the completion of (1)-(7), and in coordination with the attending veterinarian, the research team *may* resume animal work, with required veterinary presence *for at least three* surgical sessions to monitor anesthetic administration, animal recovery, and compliance with aseptic techniques.
9. In addition to routine PAM inspections, unannounced veterinary and additional PAM inspections will be conducted during procedures and in laboratory spaces until consistent compliance is demonstrated, for a period of no less than one year.

10. Report any adverse or unanticipated events promptly to the attending veterinarian, who must be consulted (i.e. spoken with in person or via phone) before any further experimental work proceeds on new animals.

During the review, the Committee also identified a protocol deviation concerning an unapproved change in analgesic. Specifically, Buprenorphine-XR (Ethiqa) was administered in place of the protocol-approved buprenorphine (0.05 mg/kg) without a prior IACUC amendment or VVC approval. In addition, documentation of analgesic dosing and administration was not maintained. This drug was not used in the experiments related to this adverse event.

Institutional Commitment and Oversight
As noted above, the IACUC is requiring additional training and increased oversight of this research group through additional PAMs along with unannounced drop-ins by the AV to ensure compliance. In addition, the IACUC will be more attentive to the maintenance of health records including peri- and post-operative recordkeeping, including anesthetic monitoring, surgical details, and recovery observations and drug usage reporting.

Conclusions
Following the report of the adverse event, the IACUC conducted a thorough review to evaluate the event and identify potential causes. The IACUC was unable to determine a definitive cause of death of the animals involved. Immediate action was taken to suspend all animal research under any IACUC-approved protocol involving this research team. Since the IACUC investigation, both the research group and IACUC have implemented corrective and preventative actions to minimize the risk of further animal welfare concerns.

Please let me know if there are any questions or concerns.

Sincerely,
(b) (6)

Ken Fridley, Ph.D., F.ASCE
Vice President for Research and Economic Development

Ware, Teagan (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, December 5, 2025 1:59 PM
To: (b) (6)
Cc: Fridley, Kenneth J.; (b) (6).; OLAW Division of Compliance Oversight (NIH/OD); Institutional Animal Care and Use Committee
Subject: RE: ODU [D16-00110 (A3172-01)] Adverse event report

Good afternoon,

Thank you for providing this final report for OLAW case **A3172-M.** We will send an official response soon.

Best,
Teagan

Teagan Ware, MS, PMP
Animal Welfare Program Analyst
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
6705 Rockledge Drive (RKL 1), MSC 7983

Phone: 301-435-2390
Email: teagan.ware@nih.gov

From: (b) (6)
Sent: Friday, December 5, 2025 1:44 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Fridley, Kenneth J. <kfridley@odu.edu>; (b) (6) Institutional Animal Care and Use Committee <IACUC@odu.edu>
Subject: [EXTERNAL] ODU [D16-00110 (A3172-01)] Adverse event report

Please find attached the ODU IACUC (D16-00110 (A3172-01)) report on an adverse event previously reported by me, by phone on Nov 14, 2025 to your office. As noted in that preliminary report this work was funded by DoD.

Please let me know if there are any questions or if additional information required.

Thanks

(b) (6)

(b) (6)

A3172-M

Initial Report of Noncompliance

By: J. Tubbs

Date: **11/14/2025** Time: 822A

Name of Person reporting: (b) (6)
Telephone #: (b) (6)
Fax #:
Email:

Name of Institution: Old Dominion University
Assurance number: A3172-01

Did incident involve PHS funded activity? Dod funded
Funding component:
Was funding component contacted (if necessary): _____

What happened?
October 6th, had 11 of 20 mice died during an experimental procedure, root case assumed to be an anesthesia issue, adverse form filed with IACUC, research paused, root cause unknown at this time.

Species involved: mice
Personnel involved: research personnel
Dates and times: Oct 2025
Animal deaths: yes

Projected plan and schedule for correction/prevention (if known): _____

Projected submission to OLAW of final report from Institutional Official:
60-90d

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Case #_____