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

November 8, 2024

Re: Animal Welfare Assurance
A3281-01 [OLAW Case 2Y]

P. Srirama Rao, Ph.D.
Vice President for Research and Innovation
Virginia Commonwealth University
800 East Leigh St.
Biotech One - (b) (4)
Richmond, VA 23219

Dear Dr. Rao,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your final report, dated October 22, 2024, of an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Virginia Commonwealth University. Initial notification was provided by phone on October 1, 2024. According to the information provided, OLAW understands that on September 16, 2024, a rabbit was premedicated by a licensed veterinary technician (LVT) with Ketamine and Dexmedetomidine as part of the standard anesthesia protocol for terminal data collection. The rabbit was intubated and transferred to the operating table. The animal was then connected to the ventilator where 3% isoflurane gas anesthesia was initiated. At this point, the end-tidal CO2 began to drop from 40 mm Hg to 32-36 mm Hg. The isoflurane was discontinued, however, the end-tidal CO2 continued to fall to 26 mm Hg. In response, 2.5 ml of atipamezole was administered. The animal's vital signs stabilized; however, the animal began to wake up. The animal was then put on 5% isoflurane gas. The animal began to destabilize again, so another 2.5 ml dose of atipamezole was administered, and isoflurane was discontinued. To stabilize the respiratory rate, the LVT attempted to administer Dopram but mistakenly injected 0.5 ml of xylazine. The animal went into respiratory depression and cardiac arrest. The animal did not recover. A Senior LVT, did not effectively communicate the situation to the on-call veterinarian. The veterinarians were on their way to work and not on-site at the time of the call. Although the animal was part of a PHS-funded research project, the direct costs, including animal expenses, per diem, and anesthesia support services, were reimbursed using internal DAR funds, reversing the charges to the PHS funds. As a result, there was no financial impact on the grant.

Corrective and preventive actions:

1. Enhanced education and training will be conducted by veterinary staff for all four LVTs. The LVT involved in the incident will receive mentorship from senior LVTs.
2. LVTs will now be required to notify the on-call veterinarian when they are ready to induce anesthesia.
3. Signs will be created and posted in the surgical suite to make critical care information more visible and accessible.
4. Establish and enforce a clear escalation process requiring LVTs to promptly contact the on-call veterinarian at the first sign of a critical issue beyond their expertise.
5. It is recommended to gradually increase the concentration of isoflurane gas anesthesia instead of starting directly at 5%, as rabbits tend to hold their breath when exposed to higher levels of isoflurane.

6. Researcher-provided drugs used during the pre-operative period will be stored in clearly labeled bags in the Surgical Prep area. Researcher-provided Atipamezole will be allowed in the Surgical OR space as an adjunct CPR drug, alongside the DAR CPR drugs in the OR crash cart. Clear labeling and careful organization will help minimize confusion, especially in high-stress situations.

It is understood that you have self-reported this incident to your USDA Veterinary Medical Officer.

Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate this incident, provide corrective measures, and prevent recurrence. OLAW concurs that the incident warranted reporting. We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

BRENT C. MORSE -S

Digitally signed by BRENT C. MORSE -S
Date: 2024.11.08 13:55:21 -05'00'

Brent C. Morse, DVM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC contact

(b) (6)

A3281-24

Virginia Commonwealth University

Office of the Vice President for Research and Innovation

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Box 980568
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P. Srirama Rao, Ph.D.
Vice president for research and innovation

October 22, 2024

Brent Morse, D.V.M., Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
(301) 496-7163

VCU Animal Welfare Assurance number D16-00180 (A3281-01)

Dear Dr. Morse:

Virginia Commonwealth University, in accordance with Assurance D16-00180 (A3281-01) and PHS Policy IV.F.3., submits this report of noncompliance involving the death of a rabbit due to a veterinary technician administering the incorrect drug. This incident was discussed and reported to you during a Zoom meeting on October 1, 2024.

Description of Incident:

On September 16, 2024, the rabbit was premedicated by a licensed veterinary technician (LVT) in the University's Division of Animal Resources (DAR) with Ketamine and Dexmedetomidine via intramuscular route as part of the standard anesthesia protocol for terminal data collection. The rabbit was intubated and transferred to the operating table. The animal was then connected to the ventilator where 3% isoflurane gas anesthesia was initiated. At this point, the end-tidal CO2 began to drop from 40 mm Hg to 32-36 mm Hg. The isoflurane was discontinued, however, the end-tidal CO2 continued to fall to 26 mm Hg. In response, 2.5 ml of the anesthetic reversal agent atipamezole was administered. The animal's vital signs stabilized, however, the animal began to wake up. The animal was then put on 5% isoflurane gas. The animal began to destabilize again, so another 2.5 ml dose of atipamezole was administered, and isoflurane was discontinued. To stabilize the respiratory rate, the first LVT attempted to administer Dopram but mistakenly injected 0.5 ml of Rompun (Xylazine), confused between the trade names of Dopram and Rompun. The animal went into respiratory depression and cardiac arrest. Chest compressions were initiated and two doses of epinephrine were administered, but the animal did not recover. The second LVT was in and out assisting the first LVT during the procedure. Both LVTs performed CPR, and the second LVT contacted a Senior LVT, who did not effectively communicate the situation to the on-call veterinarian. The veterinarians were on their way to work and not on-site at the time of the call.

According to the information collected above, the following concerns were identified:

1. The LVT mistakenly administered Rompun instead of Dopram, a respiratory stimulant. This error directly contributed to the fatal outcome and highlights the risk of confusion between brand names during emergency situations.

2. Neither DAR LVT contacted the on-call veterinarian when the animal's condition first deteriorated following the initiation of isoflurane gas anesthesia, and the Senior LVT also failed to communicate effectively with the veterinarian regarding the situation. This indicates a breakdown in escalation procedures for seeking guidance, especially since the veterinarians were en route to the facility and not on-site when the call was received. While LVTs are trained to manage anesthesia and initiate emergency care during surgeries, there is a need for a clear process for alerting the on-call veterinarian when an animal becomes unstable. Developing a decision tree could provide LVTs with clear guidance on when to involve veterinarians during emergencies.

3. Rabbits often hold their breath when exposed to higher concentrations of isoflurane (5%), which can result in a decreased respiratory rate and hypercapnia.

4. The incident reveals possible gaps in the training of LVTs, particularly in responding to anesthesia-related emergencies.

Corrective action plan:

1. Enhanced education and training:
    a. All four LVTs met with the DAR Clinical Veterinarian to discuss strategies for minimizing similar errors in the future.
    b. The LVT involved in the incident will receive mentorship from senior LVTs during upcoming surgeries, focusing on improving anesthetic intervention skills. This hands-on guidance will provide additional support and training.
    c. Veterinary staff will conduct periodic tabletop exercises to practice emergency response procedures during surgeries. These scenarios will encourage discussion of optimal responses without the pressure of real-time emergencies, allowing staff to share insights from their diverse experiences in both research and general practice.

2. New guidance and signage:
    a. LVTs will now be required to notify the on-call veterinarian when they are ready to induce anesthesia. This ensures that the veterinarian is aware the procedure is starting and can be prepared to provide guidance or consultation, either in person or over the phone, if any issues arise. Signs will be created and posted in the surgical suite to make critical care information more visible and accessible. These signs will also be shared with the IACUC for review.
    b. Establish and enforce a clear escalation process requiring LVTs to promptly contact the on-call veterinarian at the first sign of a critical issue beyond their expertise. The process should include a decision tree or flowchart outlining when and how to communicate with veterinarians in various scenarios.

3. Improved clinical management:
    a. It is recommended to gradually increase the concentration of isoflurane gas anesthesia instead of starting directly at 5%, as rabbits tend to hold their breath when exposed to higher levels of isoflurane.
    b. Researcher-provided drugs used during the pre-operative period will be stored in clearly labeled bags in the Surgical Prep area. Researcher-provided Atipamezole will be allowed in the Surgical OR space as an adjunct CPR drug, alongside the DAR CPR drugs in the OR crash cart. Clear labeling and careful organization will help minimize confusion, especially in high-stress situations.

Although the animal was part of a PHS-funded research project, the direct costs, including animal expenses, per diem, and anesthesia support services, were reimbursed using internal DAR funds, reversing the charges to the PHS funds. As a result, there was no financial impact on the grant.

We deeply regret this incident and have taken specific corrective actions to enhance our program and prevent future occurrences. We self-reported this incident to our USDA Veterinary Medical Officer to ensure awareness of the adverse event, and we will implement corrective actions to prevent similar events in the future. The IACUC will be briefed on these corrective actions at their next full committee meeting.

We appreciate your consideration of VCU's efforts to minimize future incidents. VCU remains committed to animal welfare and acknowledges its ethical responsibilities in ensuring the well-being of research animals and complying with the PHS Policy on the Humane Care and Use of Laboratory Animals.

Sincerely,

(b) (6)

P. Srirama Rao, Ph.D.
Vice President for Research and Innovation

Ware, Teagan (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, October 28, 2024 8:37 AM
To: (b) (6)
Cc: Srirama Rao; (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: [EXTERNAL] Follow-up noncompliance letter (VCU Assurance# D16-00180/A3281-01)

Good morning,

Thank you for providing this final report for OLAW case **A3281-2Y**. 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

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

From: (b) (6)
Sent: Sunday, October 27, 2024 1:37 PM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Srirama Rao <psrao@vcu.edu>; (b) (6)
Subject: [EXTERNAL] Follow-up noncompliance letter (VCU Assurance# D16-00180/A3281-01)

Dear Dr. Morse,

Please find attached the follow-up noncompliance letter, signed by VCU's Institutional Official, Dr. Rao, who is copied on this email. During our Zoom meeting on October 1st, I shared some preliminary information about this. The attached report now includes a comprehensive overview of the issue and outlines the actions taken by the VCU Division of Animal Resources and IACUC. Additionally, we have self-reported this incident to our USDA Veterinary Medical Officer to ensure full awareness of the adverse event.

We sincerely appreciate your attention to this matter. VCU remains fully committed to compliance with the Public Health Service Policy on the Humane Care and Use of Laboratory Animals and the Guide, while maintaining our strong dedication to animal welfare.

If you have any questions or require further information, please feel free to contact me at (b) (6) or via email at (b) (6)

Thank you for your time and attention.

Best regards,

(b) (6)

A3281-2Y

Initial Report of Noncompliance

By: BCM

Date: **10/1/2024** Time: 10:30

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

Name of Institution: __ Virginia Commonwealth Univ._____
Assurance number: ___A3281_____

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

What happened: Vet Tech administered isoflurane for research procedure. Rabbit became "critical". Administered atipamezole. Rabbit improved. Tech increased isoflurane, then rabbit crashed again. Attempted to administer dopram but gave xylazine instead. Rabbit crashed again and was euthanized. Vet not alerted.

Species involved: Rabbit
Personnel involved: Vet Tech
Dates and times: 9/16/2024
Animal deaths: euthanized

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

Vet Tech being retrained and policy of notifying Vet at outset of medical problems being considered.

Projected submission to OLAW of final report from Institutional Official:

< 60 days.

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Case #_____