



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Laboratory Animal Welfare  
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Bethesda, Maryland 20892-6910  
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

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6700B Rockledge Drive, Suite 2500  
Bethesda, Maryland 20817  
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June 15, 2020  
Revised Response

Re: Animal Welfare Assurance  
#A3245-01 (OLAW Case 3V)

Dr. Melur K. Ramasubramanian  
Vice President for Research  
Professor, Mechanical Engineering  
University of Virginia  
Box 400301  
Charlottesville VA 22904-4301

Dear Dr. Ramasubramanian,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your June 12, 2020 revised letter responding to OLAW's March 23, 2020 request for additional information regarding an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Virginia-Charlottesville. According to the information provided, OLAW understands that 281 mice were impacted by the non-compliance. OLAW also understands that animal handlers were retrained by the Office of Animal Welfare (OAW) and in addition, OAW will continue performing random and scheduled audits, laboratory visits and post-approval monitoring of the laboratories in which the non-compliances were identified. Documentation including call schedules, anesthetic records and vivarium inspection logs were provided by the Principal Investigators to OAW in order to verify the corrective action plan was implemented as required. Clarification was provided in reference to there being one violation under both the animal use protocol and surgery policy. Experiments involving impacted animals were repeated using funds unrelated to NIH funding sources.

OLAW appreciates the prompt consideration of this matter by University of Virginia-Charlottesville, which is consistent with the philosophy of institutional self-regulation. Based on the information provided, OLAW is satisfied that appropriate steps have been taken to investigate this incident. We appreciate being informed of this matter and please contact us with any further questions or concerns.

Sincerely,

Nicole L.  
Lukovsky-  
akhsanov -S

Digitally signed by Nicole  
L. Lukovsky-akhsanov -S  
Date: 2020.06.15 15:20:25  
-04'00'

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

cc: IACUC contact



Vice President for Research

June 12, 2020

Dr. Nicole Lukovsky-Akhsanov, DVM, MPH, DACLAM  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
6700B Rockledge Drive, Suite 2500, MSC 6910  
Bethesda, Maryland 20892-6910

Re: #A3245-01 (OLAW Case 3V)  
REVISED RESPONSE

Dear Dr. Lukovsky-Akhsanov,

On behalf of the University of Virginia IACUC, this correspondence is in response to your request for additional information related to Case A3245-3V (UVA 2019-Q and 2019-R) as referenced in your letter dated March 23, 2020 and requested during the teleconference on June 11, 2020.

Approximately 281 mice were impacted by the non-compliance event. The IACUC determined that two animal handlers deviated from approved animal use protocols when they failed to administer adequate post-operative analgesia as stated in the approved protocols. By failing to provide adequate post-operative analgesia and appropriate documentation, the IACUC also considered this incident to be a deviation from the rodent surgery policy. The one violation was a deviation under both the animal use protocol and surgery policy. The IACUC suspended the animal handling privileges for both of the individuals. Experiments involving the impacted animals were repeated; however, the funding for those experiments were unrelated to NIH sources.

You also asked that we "describe the monitoring plan in place by your organization to ensure animal handler, PI, lab staff compliance with the resolution terms as agreed upon with the IACUC." The approach taken was and continues to be multifaceted. The PIs are responsible for ensuring that their animal handlers adhere to IACUC policies and procedures. The PIs work closely together and have joint laboratory meetings where they will continue to review animal concerns and topics with the laboratory staff as well as at departmental meetings. The PIs stressed to their staff that there was a zero tolerance policy in effect going forward for anyone not being familiar with the protocols and following them exactly, and each animal handler was required to provide their signature verifying that they read, understood, and agreed. A "call schedule" was created and shared with the vivarium supervisor. The PI indicated in the corrective action plan that he would audit anesthetic logs and inspect the surgery cage cards and vivaria on a routine basis.

The husbandry and veterinary staff monitor the animals daily and report any potential non-compliance issues to the OAW for IACUC review and deliberation. The IACUC reviewed the documents provided by the PI during the corrective period of the incident. For example, the PI provided the minutes for several of his laboratory meetings with his staff. The Office of Animal Welfare (OAW) retrained the animal handlers on the proper methodologies for completing surgery cage cards and anesthetic records. The IACUC will continue to perform semi-annual inspections of vivaria spaces housing these animals and of laboratory spaces where these animals are taken. OAW will continue to periodically perform random

and scheduled surgery cage card audits, laboratory visits, and Post-Approval Monitoring meetings with these laboratories. The OAW reviewed the call schedule, anesthetic records, and vivaria inspection log provided by the PI in order to verify that the corrective action plan was being followed as described.

Should you have any additional questions regarding the resolution of this case, please let me know.

Sincerely,

(b) (6)

Melur K. (Ram) Ramasubramanian  
Vice President for Research

cc:

(b) (6)

Carl E. Creutz, Chair, Animal Care and Use Committee  
Angela Gamble, Director, Office of Animal Welfare  
Silvia LaRue, Director, ACUC Office

**University of Virginia**  
**Animal Welfare Compliance Report**  
**PHS Assurance # A3245-01**

A preliminary email notification was sent to Dr. Brent Morse of OLAW by Angela Gamble, Director of the Office of Animal Welfare. It was understood that a full report would follow IACUC investigation. This document is a summary of the incident, actions taken, and final resolution.

**UVA Compliance Case #:** 2019-Q (PI #1)  
2019-R (PI #2)

<b>Nature of Incident(s):</b>	Failure to adhere to approved protocols resulting in inadequate post-operative care; failure to maintain appropriate animal-related records (mice)
<b>Summary of Incident:</b>	During a routine audit of surgery cage cards, the Office of Animal Welfare (OAW) discovered several incomplete surgery cage cards related to documenting post-operative observations and analgesia administration. The animal handlers involved perform animal work for both PIs. The OAW Director met with the laboratory staff and reviewed the IACUC expectations for survival surgery and surgery cage card use. Upon further investigation and an additional meeting with the PIs and laboratory staff, OAW found that post-operative analgesia was not administered as documented on the surgery cage cards nor in accordance with the approved protocols. The PIs were instructed to modify their protocols to clearly describe the post-operative analgesia based on surgery type, and once approved, they must follow the approved protocol.
<b>Action taken by IACUC:</b>	At the next convened meeting, the IACUC discussed the incident. They determined that the failure to administer analgesia to animals, deviations from the protocols, and violation of the IACUC rodent survival surgery policy was significant and required correction. It appeared that the PIs were not providing adequate oversight and or training. The IACUC voted to suspend the two primary animal surgeons for a minimum of 60 days. The PIs were sent a joint letter from the IACUC regarding their concerns and required a written corrective action plan. The letter also required that the PIs meet with a sub-committee of the IACUC to further discuss the incident and the PIs' plans for resolution.

<p><b>Action taken by PIs jointly:</b></p>	<p>The PIs provided a joint written corrective action plan. The PIs acknowledged that it was their responsibility to ensure that experiments were conducted and adhered to their protocols and apologized for the serious lapses in oversight and animal care. They indicated that their long-term surgeon retired and they had assumed that practices had remained the same. The surgeon change was coincident with the retirement of their long-term laboratory manager and all of their postdoctoral fellows. The PIs stated that they were not aware of any clinical signs of pain or distress being reported by the veterinary staff and the surgeons did not report any problems; therefore, they had no reason to question practices or to suspect that deviations from established procedures had occurred.</p> <p>Following the second meeting with OAW, the PIs met with their animal handlers on several occasions to resolve the incident. The animal handlers were told that no deviations from the protocol were allowed or tolerated, and all animal handlers must be familiar with the protocol(s) and follow them exactly. Each animal handler was required to document their reading and understanding of the protocols and ACUC policies cited. The role of the lab managers were was reenforced and they were tasked with performing additional oversight: reviewing the controlled substance logs and surgical records weekly for completeness. The PIs will perform the same task monthly. The PIs will also discuss animal related issues with their collaborators as part of their weekly group meeting. They increased continual oversight of all animal procedures being performed to ensure they align with the approved protocols. Each laboratory member will be assigned a specific procedure to review during each lab meeting. The laboratory established a call schedule for members of the laboratory and shared it with the vivarium staff.</p> <p>The IACUC sub-committee met with the PIs and reviewed their concerns and received assurance from the PIs that they will improve compliance, oversight, and training. They reviewed portions of their corrective action plan as previously submitted and reviewed by the IACUC. The PIs indicated that they will also visit the vivarium on a monthly basis to inspect surgery cage cards and animal welfare. After the 90 day suspension, the PIs may petition the IACUC for reinstatement of animal privileges for the two surgeons.</p>
<p><b>Action taken by IACUC:</b></p>	<p>The protocols were approved as modified. The IACUC felt that the PIs responded appropriately. Once the 90 day period was complete, the IACUC reviewed and approved the petition for reinstatement. No further action was deemed necessary.</p>



<b>Decision/Resolution:</b>	The IACUC considered the incident resolved.
<b>Federal Funding:</b>	PI #1: 1R01 DK085259; 1R01 DK105133 PI #2: R01 DK114366 A1
<b>Notification of Final Disposition:</b>	<input checked="" type="checkbox"/> IO <input checked="" type="checkbox"/> OLAW

## Morse, Brent (NIH/OD) [E]

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**From:** Maclarty, Arthur (NIH/NEI) [E]  
**Sent:** Thursday, January 16, 2020 10:50 AM  
**To:** List VETMED-L  
**Subject:** 2020 AVMA Guidelines for the Euthanasia of Animals  
**Attachments:** 2020\_Euthanasia\_Final\_1-15-20.pdf

Below is a synopsis of the changes/updates/clarifications in the updated 2020 AVMA Euthanasia Guidelines. The notes were collected from the Jan 16 webinar presented by (b) (6). The points are further explained in the 2020 edition of the AVMA Guidelines for the Euthanasia of Animals attached.

1. Clarified the definitions of a sedative vs an anesthetic
  - a. Immobilizing, Tranquilizing, and Sedative agents should not be relied upon to produce a truly unresponsive, disconnected, unconscious state.
2. Small Laboratory and Wild-Caught Rodents section
  - a. The flow rate for CO2 euthanasia systems has been amended from 10-30% to 30-70% of the chamber volume/min.
  - b. Still use an uncharged chamber.
3. Rabbits
  - a. Acceptable with Conditions
    - i. Use of CO2 is an uncharged chamber and a flow rate of 50-60% of chamber volume/min.
    - ii. Physical method of Penetrating and Non-Penetrating Captive Bolt
4. Bovids section
  - a. Expansion to include Bison and Water Buffalo
5. Small Ruminants section
  - a. Expansion to include Farmed Cervids and Camelids
  - b. Goat Kids (< 3 weeks of age)
    - i. Acceptable with conditions – the use of CO2 at a flow rate of 70% volume/min over 5 minutes with a 10 minutes dwelling time
6. Farmed Animals for Food or Fiber section
  - a. Updated pictures for physical methods
    - i. Captive bolt placement sites
    - ii. Turkey captive bolt placement
7. Equids section
  - a. Under a surgical plane of anesthesia, the following injectables are now Adjunctive Methods to eliminate pentobarbital contamination of carcasses
    - i. Saturated solution of potassium chloride IV or IC
    - ii. Saturated solution of magnesium sulfate IV
    - iii. Lidocaine intrathecally
8. Avian section

- a. Eggs, Embryos, and Neonates
  - i. Embryos changed from 50% to 80% of incubation stage when embryos achieve the potential for perception
  - ii. Applied across all avians with consideration for species specific differences in development

9. Laboratory Fish, Amphibians, and Aquatic Invertebrates section

- a. Under Non-Inhaled section
  - i. MS222 – 30 minutes exposure following the loss of rhythmic operculum movement
- b. Physical section
  - i. Blunt force trauma and captive bolt/pithing of fin fish
  - ii. Pictures added for correct placement of captive bolt or blunt force trauma site
- c. Aquatic Invertebrates
  - i. Proper use of magnesium salts or ethanol

10. Zoologic and Free Ranging Non-domestic Animals

- a. New – captive bolt or firearm for Crocodilians and other large reptiles
- b. Pictures added for correct placement of captive bolt or firearm site

11. Appendices

- a. (1) – lists agents and methods by species
- b. (2) – Agents and methods that are unacceptable as a primary agent/method
- c. (3) – Figures/Pictures

Arthur J. MacLarty, DVM  
Chief, Veterinary Services  
Building 49 Central Animal Facility  
National Eye Institute  
49 Convent Dr., Room (b) (4)  
Bethesda, MD 20892  
Office: (b) (6)  
Cell: (b) (6)



**Morse, Brent (NIH/OD) [E]**

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Thursday, January 23, 2020 12:09 PM  
**To:** (b) (6) OLAW Division of Compliance Oversight (NIH/OD); Wolff, Axel (NIH/OD) [E]  
**Cc:** (b) (6) Gamble, Angela (adr8s); Ramasubramanian, Melur K (mkr5a)  
**Subject:** RE: UVA-OLAW Compliance report 2019-Q and 2019-R

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

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**From:** (b) (6)  
**Sent:** Thursday, January 23, 2020 11:09 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>  
**Cc:** Ward, Joan (NIH/OD) [E] <wardjoa@od.nih.gov>; (b) (6) Gamble, Angela (adr8s) <adr8s@virginia.edu>; Ramasubramanian, Melur K (mkr5a) <mkr5a@virginia.edu>  
**Subject:** UVA-OLAW Compliance report 2019-Q and 2019-R

Dr. Axel Wolff, Director of Compliance Oversight Office of Laboratory Animal Welfare National Institutes of Health RKL 1, Suite 360, MSC 7982  
6705 Rockledge Dr., Bethesda, MD

Dr. Wolff:

I attach a compliance report from our IACUC. These are for our case 2019-Q and 2019-R.

In this case, the IACUC has investigated thoroughly, taken appropriate action and the committee has determined that this matter is now resolved to their satisfaction.

I have reviewed the report and I concur with the committee response and final determination.

Best regards,

(b) (6)  
For Melur Ramasubramanian

(b) (6)

(b) (6)

A3245-3V

**Morse, Brent (NIH/OD) [E]**

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**From:** Morse, Brent (NIH/OD) [E]  
**Sent:** Thursday, January 09, 2020 7:14 AM  
**To:** Gamble, Angela (adr8s); OLAW Division of Compliance Oversight (NIH/OD); Wolff, Axel (NIH/OD) [E]  
**Cc:** (b) (6)  
**Subject:** RE: preliminary notification - UVA (Assurance A3245-01): 2019-P and 2019-Q/R

Thank you for submitting this report. We will open two separate cases and await the final reports.

Best regards, Brent Morse

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

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**From:** Gamble, Angela (adr8s) [mailto:adr8s@virginia.edu]  
**Sent:** Wednesday, January 08, 2020 5:48 PM  
**To:** Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>  
**Cc:** Gamble, Angela (adr8s) <adr8s@virginia.edu>; (b) (6)  
**Subject:** preliminary notification - UVA (Assurance A3245-01): 2019-P and 2019-Q/R

Dear Drs. Wolff and Morse,

This is to provide preliminary notification that the University of Virginia IACUC (PHS Assurance #A3245-01) has identified two significant deficiencies, one of which involves two researchers. The two separate events occurred at the end of 2019, and the events are currently under investigation and review by the IACUC. We are working with each PI towards resolution, and we will send you a complete report for each event once it has been resolved. The reports will likely be sent separately based on the individualized timeline of resolution. The two separate events are listed below by IACUC Tracking Number.

- 2019-P: Use of an expired anesthetic solution for euthanasia of rodents
- 2019-Q and 2019-R: This single event has two IACUC Tracking Numbers due to the dual involvement of two separate investigators. The investigators share surgical animal handlers and it appears that post-operative care was inadequate and appropriate animal records were not maintained.

Should you have any questions or concerns prior to receiving our final report, please do not hesitate to contact me.

Sincerely,  
Angela Gamble

Angela Gamble  
University of Virginia  
Director, Office of Animal Welfare  
Charlottesville, VA 22908  
PH: (b) (6)