



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) 402-7065

August 7, 2019

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

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 August 1, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Virginia, following up on an initial report on May 28, 2019. According to the information provided, OLAW understands that expired anesthetic had been used to euthanize mice and that dry ice was being used to generate CO2 for euthanasia.

The corrective action consisted of the Institutional Animal Care and Use Committee (IACUC) directing the Principal Investigator to discard the expired drug and to stop using dry ice. The PI acquired a euthanasia chamber with a flow meter and compressed CO2, the expired drugs were discarded, and use of a log book was implemented to track drug expiration dates. The laboratory staff was trained on these new procedures and the protocol was amended to clarify euthanasia procedures. The IACUC counseled the PI to never use expired anesthetics or dry ice.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the IACUC to comply with the PHS Policy.

Sincerely,

(b) (6)

Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare

cc: IACUC Chair
Director, Office of Animal Welfare

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-D

Nature of Incident(s):	Use of expired anesthesia for euthanasia (mice) Protocol violation – use of an unapproved method of euthanasia (mice)
Summary of Incident:	<p>During the semi-annual inspection, the IACUC found a vial of expired anesthetic solution that had been used beyond the expiration date to euthanize animals.</p> <p>The inspectors also found that the same PI was using dry ice as a method of generating source of CO₂ for euthanasia. The animals were not in direct physical contact with the dry ice.</p>
Action taken by IACUC:	<p>The IACUC discussed the incident at the Program Review meeting and determined that both issues would be considered significant deficiencies. The IACUC sent the PI a letter reminding him that he is prohibited from using expired anesthesia for any purpose. He was required to properly dispose of the expired materials and to provide a written corrective action plan to prevent reoccurrence. Due to the potential impact on animal welfare, the IACUC agreed that this was a significant deficiency.</p> <p>The PI was reminded that IACUC policy prohibits the use of dry ice as a method of producing CO₂ for euthanasia, and CO₂ must be dispensed from a compressed gas cylinder at a controlled rate. The IACUC considered this an unapproved method of euthanasia a protocol violation and therefore a significant deficiency.</p>

Action taken by PI:	The PI provided a written corrective action plan to improve compliance which included the disposal of the expired anesthetic and the installation of a new euthanasia chamber with flow meter and compressed CO ₂ . The laboratory made improvements in their controlled drug recordkeeping to also track expiration dates more thoroughly. The dates will be inspected before use to ensure that all components are in date prior to use. He reviewed these changes with his animal handlers. The PI trained his animal handlers on the operation of the new euthanasia chamber to include the correct flow rate setting as well as chamber occupancy as well as the IACUC policy details. The PI modified the animal use protocol to ensure that all methods of euthanasia were explained adequately.
Action taken by IACUC:	The IACUC approved the protocol modifications and re-enforced the regulations with the PI to ensure that he understood that the use of expired anesthetics are never permitted, including when performing euthanasia and that dry ice is never permitted for generating CO ₂ . The IACUC felt that the PI responded appropriately and no further action was deemed necessary. The protocols were approved as modified.
Decision/Resolution:	The IACUC accepted the corrective action plan and considered the incident resolved. The Office of Animal Welfare verified the presence of the CO ₂ euthanasia station located in the laboratory.
Federal Funding:	R01 AR047988
Notification of Final Disposition:	<input checked="" type="checkbox"/> IO <input checked="" type="checkbox"/> OLAW <input type="checkbox"/> AAALAC

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, August 2, 2019 6:32 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: UVA OLAW Compliance Report

Thank you for these reports, (b) (6) We will send responses soon.
Axel Wolff

From: (b) (6)
Sent: Thursday, August 1, 2019 2:35 PM
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) Ramasubramanian, Melur K (mkr5a) <mkr5a@virginia.edu>; Gamble, Angela (adr8s) <adr8s@virginia.edu>
Subject: UVA OLAW Compliance Report

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 two compliance reports from our IACUC.

In these cases, the IACUC has investigated thoroughly, taken appropriate action and the committee has determined that these matters have been resolved to their satisfaction.

I have reviewed the reports and I concur with the committee responses and final determinations.

We made a preliminary report for our compliance item 2019-F. After further investigation we have determined that the animals and research involved were funded by neither NIH or NSF. A final report was sent to me as the IO but we are not submitting the final report to OLAW. We will, of course, forward that report if you wish.

Best regards,

(b) (6)

For Melur K. Ramasubramanian

(b) (6)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, May 29, 2019 6:45 AM
To: Gamble, Angela (adr8s)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: preliminary notification - UVA (Assurance A3245-01): 2019-A, 2019-D, 2019-F, and 2019-H

Thank you for these preliminary reports, Ms. Gamble. We will start new case files and look forward to receiving the final reports from the IO after the IACUC has completed its investigation.

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

From: Gamble, Angela (adr8s) <adr8s@virginia.edu>
Sent: Tuesday, May 28, 2019 2:43 PM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Gamble, Angela (adr8s) <adr8s@virginia.edu>; (b) (6)
Subject: preliminary notification - UVA (Assurance A3245-01): 2019-A, 2019-D, 2019-F, and 2019-H

Dear Dr. Morse,

This is to provide preliminary notification that the University of Virginia IACUC (PHS Assurance #A3245-01) has identified three potential significant deficiencies as a result of the recent semi-annual inspection and one significant deficiency independent of the inspection. Each item below is under investigation and review by the IACUC. We are working with the PIs towards resolution and will send you a complete report for each incident once it has been resolved. The items are listed by IACUC Tracking Number.

- 2019-A: Conducting an animal related activity without appropriate IACUC review and approval (mice)
- 2019-D: Use of an expired anesthetic and use of an inappropriate method of euthanasia (mice)
- 2019-F: Condition that *potentially* jeopardized the health or well-being of animals resulting in the *potential* for harm or death (neonatal mice)
- 2019-H: Condition that jeopardized the well-being of animals resulting in actual death (neonatal mice)

Should you have any questions or concerns prior to receiving our final reports, 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)