



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

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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

March 10, 2023

Re: Animal Welfare Assurance
#A3245-01 [OLAW Case 4V]

Dr. Melur Ramasubramanian
Vice President for Research
University of Virginia - Charlottesville
P.O. Box 400301
Charlottesville VA 22904

Dear Dr. Ramasubramanian,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 7, 2023 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 January 26, 2023. According to the information provided, OLAW understands that five mice were found dead or moribund as a result of laboratory staff not monitoring animals as required and not adhering to the endpoint criteria regarding euthanasia. Also, 17 cages had notices not to change the bedding which was found to be excessively soiled. Both findings were noncompliant with what had been described in the approved protocol and were in part due to inadequate oversight and training.

The corrective actions consisted of the Institutional Animal Care and Use Committee (IACUC) directing the Principal Investigator (PI) to amend the protocol to clearly describe the endpoint criteria and to retrain the animal handlers to recognize the clinical signs and euthanize affected mice as necessary. A protocol amendment was also required to address cage change frequency and laboratory staff was trained on appropriately changing cages and documenting this. The PI enhanced oversight of the colony, implemented laboratory meetings to discuss animal issues, and increased staff training.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of these problems. 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

University of Virginia
Animal Care and Use Compliance Report
PHS Assurance # A3245-01

The Institutional Animal Care and Use Committee (IACUC) found the following compliance issue while performing an inspection in the vivaria, and the issue was associated with NIH funds. A preliminary email notification was sent to the OLAW Division of Compliance Oversight by the Director of the Office of Animal Welfare. Devora McCoy, Program Analyst, acknowledged receipt. It was understood that a full report would be submitted following IACUC review. This document is a summary of the incident, actions taken, and final resolution.

UVA Case #: 2022-V

OLAW Case #: A3245- 4V

Nature of Incident(s):	Failure to adequately monitor animals post-procedurally as necessary to ensure well-being; failure to adhere to approved protocol for housing conditions (mice)
Summary of Incidents:	<p>Two issues were noted as occurring simultaneously. The veterinary staff reported to the Office of Animal Welfare that five mice were found in poor condition or dead. Upon further investigation, it was found that the laboratory staff did not monitor the animals post-infection at the frequency stated in the protocol. Signatures of morbidity listed in the protocol did not correlate with the scoring being performed, and animals were not euthanized in accordance with the protocol humane endpoint criteria.</p> <p>During the inspection of the vivaria, members of the IACUC found approximately 17 cages were marked as “do not change bedding” and were found excessively soiled. The non-standard husbandry was not approved and considered a significant protocol deviation. The cages were not being changed by the laboratory animal handlers in accordance with standard practice.</p>
Action taken by IACUC:	<p>The IACUC discussed the incidents at a convened meeting. The IACUC determined that the issues were both significant protocol deviations resulting in conditions that impacted animal welfare (failure to adequately monitor) or had the <i>potential</i> to impact animal well-being (non-standard care, excessively soiled bedding).</p> <p>The IACUC required that the PI consult with the Attending Veterinarian and modify the protocol to reflect appropriate humane endpoint monitoring criteria for specific infection models and experiments. Upon approval, animal handlers must be retrained to recognize humane endpoint criteria and euthanize animals appropriately. The PI self-implemented enhanced oversight measures while the resolution was being determined, and the IACUC requested that the measures continue until all animal handlers were retrained as described.</p> <p>The IACUC required that the PI modify the protocol to provide a scientific justification for performing non-standard husbandry</p>

	<p>practices (laboratory animal handlers changing cages). Upon approval, the laboratory staff would be required to change the cages in accordance with standard change frequency and required documentation measures. The PI must ensure that the animal handlers are fully trained to change cages appropriately, at the standard frequency, and document completion. The IACUC sent a letter to the PI notifying them of the deficiencies and required a written corrective action plan to prevent reoccurrence.</p>
Action taken by PI:	<p>The PI responded to the IACUC concerns. The PI discovered performance issues with the colony manager resulting in problems associated with colony oversight, monitoring, and training of new animal handlers.</p> <p>The new animal handlers were not adequately trained in all aspects of humane endpoint monitoring and required frequency. Methods of supportive care for infected animals was not relayed appropriately to new animal handlers. As a result, the PI enhanced oversight measures including one-on-one training, routine inspections of the colony, and continued additional oversight until all animal handlers were competent. The PI instituted bi-weekly in vivo subgroup meetings to discuss current work and ensure ample monitoring coverage. The laboratory enhanced oversight of the entire colony by having all animal handlers scan the entire colony routinely. The PI requires that the colony manager to copy the PI on all potential adverse issues noticed in the colony. Following veterinary consultation, the protocol was modified to include a more detailed monitoring system including increased monitoring during specific infection periods. Animal handlers were retrained in accordance with protocol revisions.</p> <p>The PI updated the protocol to justify the use of non-standard husbandry practices during specific time points of infection and for specific experiments. The PI provided assurance that animal handlers would be trained appropriately. The PI determined that the cages were not changed frequently due to insufficient training of new animal handlers and miscommunication by the colony manager. The corrective actions employed to resolve the monitoring deficiency will be used to resolve the non-standard husbandry issues (bi-weekly meeting, enhanced oversight, enhanced training).</p>
Action taken by IACUC:	<p>The protocol modifications were reviewed and approved by the IACUC. The IACUC felt that the PI responded appropriately and no further action was deemed necessary.</p>
Decision/Resolution:	<p>The IACUC accepted the corrective action plans as submitted by the PI and considered the incident resolved.</p>
Federal Funding:	R35 GM138381
Notification of Final Disposition:	<input checked="" type="checkbox"/> IO <input checked="" type="checkbox"/> OLAW
Institutional Official: Dr. Melur K. Ramasubramanian	<p>(b) (6)</p> <p>Date: March 7, 2023</p>

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, March 8, 2023 11:02 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: UVA Compliance Report 2022-V and Preliminary Notification

Good morning (b) (6)

Thank you for sending us this final report for case A3245-4V and we will send an official response soon.

Best,
Devora

Devora McCoy, BS, MBA ([pronunciation](#))
Program Analyst
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

Phone: 301-435-2390
Email: devora.mccoy@nih.gov

From: (b) (6)
Sent: Tuesday, March 7, 2023 4:08 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>; McCoy, Devora (NIH/OD) [E] <devora.mccoy@nih.gov>
Cc: (b) (6)
Subject: [EXTERNAL] UVA Compliance Report 2022-V and Preliminary Notification

To whom it may concern: Please find attached UVA's final compliance report (see attached preliminary notification).

Please let me know if I can be of further assistance,

(b) (6)

A3245-4V

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, January 26, 2023 1:40 PM
To: [REDACTED] (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: preliminary notification - UVA (Assurance A3245-01); 2022-V

Good afternoon [REDACTED] (b) (6)

Thank you for sending us this preliminary report and we look forward to receiving the final report once completed. This report has been assigned OLAW case number **A3245-4V**, so please reference this number when sending the final report.

Best,
Devora

Devora McCoy, BS, MBA (pronunciation)
Program Analyst
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

Phone: 301-435-2390
Email: devora.mccoy@nih.gov

From: [REDACTED] (b) (6)
Sent: Thursday, January 26, 2023 12:59 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>
Cc: [REDACTED] (b) (6)
Subject: [EXTERNAL] preliminary notification - UVA (Assurance A3245-01); 2022-V

Dear OLAW Division of Compliance Oversight,

This is to provide preliminary notification that the University of Virginia IACUC (PHS Assurance #A3245-01) identified a significant deficiency related to mice. The UVA tracking number is 2022-V.

The issue is currently under investigation and review by the IACUC. We are working towards resolution and will send a separate compliance report once resolved. It appears that a researcher may have failed to adequately monitor animals post-procedurally as necessary to ensure well-being and performed unapproved husbandry tasks.

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

Sincerely,
[REDACTED] (b) (6)

