



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

April 11, 2024

Re: Animal Welfare Assurance
A3245-01 [OLAW Case 5H]

Frederick H. Epstein, Ph.D.
Professor and Interim Vice President for Research
University of Virginia - Charlottesville
P.O. Box 400301
Charlottesville, VA 22904

Dear Dr. Epstein,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your April 3, 2024, letter reporting a series of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Virginia, following up on an initial email notification on March 25, 2024. According to the information provided, OLAW understands that during a semiannual facility inspection, it was identified that three post-procedural mice, with incomplete surgical cage cards, were initially administered an epileptic-inducing compound and subsequently treated with an analgesic and supplemental fluid prior to surgery, without prior IACUC approval. Research personnel failed to monitor the animals post-surgically and the surgeon did not appropriately document the analgesic treatment. The PHS-supported protocol was approved for compound administration in rats but not in mice. The Director of the Office of Animal Welfare discussed the noncompliance with the Principal Investigator (PI), who was unaware that the approved protocol did not include the epileptic study in mice and the animals were immediately euthanized.

The corrective actions consisted of the IACUC voting to suspend the surgeon's animal use privileges for a minimum of two weeks, with the requirement that the surgeon complete two specific online training modules. The IACUC has since voted to reinstate the surgeon's animal use privileges following completion of the mandated training. The PI reviewed the noncompliance with the animal handlers and revised the individualized surgery logs to include the administration of local analgesics. The surgeon and animal handlers were retrained on the use of the revised surgery logs and cage cards. Upon study completion, the PI will review both the surgery cage cards and surgical logs to confirm the administration of adequate analgesia. The animal handlers will ensure that the appropriate number of post-surgical observations are conducted and documented on the surgical cage cards, with advanced planning by the laboratory to ensure adequate coverage for weekend monitoring of the animals. The PI immediately amended the protocol to include epilepsy induction and subsequent palliative care in mice and will check the protocol for potential deviations in the future. The individualized surgery logs, ongoing surgery logs and controlled substances records were reorganized to a centralized location. All animal handlers were made aware of the serious nature of the noncompliance and were required to re-read the approved protocol.

Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate, correct and prevent recurrence of the noncompliance. Your prompt and thorough resolution of this matter is commendable and consistent with the PHS Policy philosophy of monitored self-regulation. We appreciate having been informed of this matter and find no cause for further action by this Office.

Sincerely,

Neera V. Gopee -S

Digitally signed by Neera V. Gopee

-S
Date: 2024.04.11 10:31:42 -04'00'

Neera V. Gopee, DVM, PhD, DACLAM, DABT
Associate Director, Animal Welfare Policy
Office of Laboratory Animal Welfare
National Institutes of Health

cc: IACUC Chair

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

The Institutional Animal Care and Use Committee (IACUC) discovered the following compliance issue and determined that it 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. Teagan Ware, Program Analyst, acknowledged receipt and assigned an OLAW case number. 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 #: 2023-Q

OLAW Case #: A3245-5H

Nature of Incident(s):	Implementation of a significant change to the IACUC-approved protocol without proper IACUC approval; failure to monitor animals post-procedurally as necessary to ensure well-being; failure to maintain appropriate animal-related records
Summary of Incident:	During a semi-annual facility inspection, the Institutional Animal Care and Use Committee (IACUC) inspection team found three post-operative mice with incomplete surgery cage cards. The cards were incomplete for the required number of post-operative observations, and the local analgesia was not documented appropriately on the surgery cage card. Animals had been administered a compound to induce status epilepticus and subsequently treated with analgesic and supplemental fluids for several days prior to surgery. Although the approved protocol described the compound administration in rats, it was not described in the approved protocol for use in mice.
Action taken by IACUC:	Upon discovery, the Director of the Office of Animal Welfare (OAW) discussed the incident with the PI. The PI failed to realize that the seizure experiment was not described in the protocol for mice and immediately euthanized the animals. The IACUC discussed the incident at a convened meeting and determined that the incident involved several significant deficiencies: implementation of a significant change to the IACUC-approved protocol without proper IACUC approval; failure to adhere to IACUC-approved protocol for documenting the local analgesic; failure to monitor animals post-procedurally as necessary to ensure well-being; failure to maintain appropriate animal-related records. The IACUC voted to suspend the animal handling privileges of the surgeon that performed the experiments for a minimum of two weeks. The surgeon was required to complete two specified online training modules prior to reinstatement. The IACUC sent a letter to the PI and required a written corrective action plan addressing the deficiencies.

Action taken by PI:	<p>The PI responded to the IACUC concerns and provided corrective actions including enhanced oversight. According to the PI, the surgeon administered the local analgesic but failed to document the administration appropriately. The PI reviewed the concern with the animal handlers and modified the individualized surgery logs to include the local analgesic administration. All animal handlers were retrained on the use of the revised document and use of the surgery cage card. The PI will review the surgery cage cards and surgical logs at the end of experiments to ensure adequate post-operative analgesia is administered. To ensure that the required number of post-operative observations are conducted, the laboratory will plan in advance weekend coverage for post-operative animals. The PI reviewed the concerns with the animal handlers and they will ensure that the appropriate number of post-operative observations are conducted and documented on the surgery cage cards. The PI will review the surgery cage cards at the end of experiments to ensure that the correct number of post-operative observations are conducted. The PI immediately modified the animal use protocol to describe the experiment for inducing seizures and for providing supportive care in mice. The PI will ensure that the protocol is checked for possible deviations in the future. The PI reorganized the individualized surgery logs, the ongoing surgery log, and controlled substance administration records to a centralized location. The PI made all animal handlers aware of the gravity of the incident and ensured compliance from the animal handlers. All animal handlers were required to re-read the approved animal use protocol. The suspended surgeon completed the required modules and was retrained with the other animal handlers as described.</p>
Action taken by IACUC:	The IACUC felt that the PI responded appropriately, and no further action was deemed necessary. The IACUC voted to reinstate the animal handling privileges of the suspended surgeon.
Decision/Resolution:	The IACUC accepted the corrective action plans as submitted by the PI and considered the incident resolved.
Federal Funding:	R61/R33 NS112549 and R56 NS097726
Notification of Final Disposition:	<input checked="" type="checkbox"/> IO <input checked="" type="checkbox"/> OLAW
Institutional Official: Dr. Frederick H. Epstein	<div style="background-color: #cccccc; padding: 10px; display: inline-block;">(b) (6)</div>
	Date:

From: OLAW Division of Compliance Oversight (NIH/OD)
To: (b) (6)
Cc: (b) (6); Epstein, Frederick H (fhe6b); (b) (6) OLAW
Division of Compliance Oversight (NIH/OD)
Subject: RE: OLAW case # A3245-5H
Date: Wednesday, April 3, 2024 2:41:00 PM

Good afternoon,

Thank you for providing this final report for OLAW case **A3245-5H**. 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

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From: (b) (6)
Sent: Wednesday, April 3, 2024 2:32 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Cc: (b) (6)
Epstein, Frederick H (fhe6b) <fhe6b@virginia.edu>; (b) (6)
Subject: [EXTERNAL] OLAW case # A3245-5H

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

Dr. Morse:

We previously submitted an email notification on a compliance matter, UVA 2023-Q (please see email below). This preliminary notification was acknowledged by Teagan Ware and assigned OLAW case #3245-5H.

The IACUC reviewed the incident and the corrective actions and has determined that this matter is now resolved to their satisfaction.

I have reviewed their final report and I agree with their recommendations. The report is attached.

(b) (6)

From: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>

Sent: Monday, March 25, 2024 10:50 AM

To: (b) (6)

cc: (b) (6)

(b) (6)

OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>

Subject: RE: Preliminary Notification of Non-Compliance: UVA - #A3245-01 (Case #2023-Q)

Good morning,

Thank you for providing this preliminary report, which has been assigned OLAW case **A3245-5H**. Please reference this case number when providing any updates or the final report for this incident.

Best,

Teagan

Teagan Ware, MS, PMP

Animal Welfare Program Analyst

Division of Compliance Oversight

Office of Laboratory Animal Welfare

A3245-SH

Ware, Teagan (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, March 25, 2024 10:50 AM
To: (b) (6)
Cc: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Preliminary Notification of Non-Compliance: UVA - #A3245-01 (Case #2023-Q)

Good morning,

Thank you for providing this preliminary report, which has been assigned as OLAW case **A3245-SH**. Please reference this case number when providing any updates or the final report for this incident.

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

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From: (b) (6)
Sent: Monday, March 25, 2024 10:43 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6)
(b) (6) Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Subject: [EXTERNAL] Preliminary Notification of Non-Compliance: UVA - #A3245-01 (Case #2023-Q)

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. The UVA tracking number is listed below. The issue is under review by the IACUC, and they are working towards resolution, and the IO will send a compliance report once adequately resolved.

- 2023-Q: Researcher failed to monitor animal post-procedurally and failed to follow approved protocol resulting in a protocol deviation (mice).

Contact me with any questions or concerns prior to receiving our final report.

Sincerely,

(b) (6)

(b) (6)