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

March 10, 2023

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

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 adverse event involving mice at the University of Virginia, following up on an initial report on January 26, 2023. According to the information provided, OLAW understands that 40 mice on an approved study became moribund or died after receiving an experimental diet containing dexamethasone at an approved dosage.

The immediate action taken upon discovery consisted of collecting blood and tissue samples from the moribund mice for toxicology and then euthanizing the animals. The Principal Investigator consulted with the veterinarian and stopped use of the special diet. The protocol was amended with a reformulated diet with a lower dose of dexamethasone.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to avoid the unexpected morbidity/mortality in this study. OLAW concurs with the actions taken by the institution to comply with the PHS Policy on Humane Care and Use of Laboratory Animals. If the reformulated diet results in future problems, please notify this Office.

Sincerely,

(b) (6)

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

cc: IACUC Chair

A3245-4U

University of Virginia
Serious Adverse Event Report

The Office of Animal Welfare recognized a serious adverse event and presented the information to the IACUC for review. The event was an *unanticipated inadvertent incident* that led to harm or endangered the well-being of animals within the animal care and use program. The research laboratory involved in the incident was fully compliant with the PHS Policy, AWA Regulations, IACUC policies, and the IACUC approved animal use protocol. A preliminary email notification of the unanticipated serious adverse event 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 event, actions taken, and final resolution. The issue was *not* deemed a compliance issue by the IACUC.

UVA Case #: 2022-U
OLAW Case #: A3245-4U

Adverse Event Classification:	*Scope*: Contained, Inadvertent Event *Sub-Category*: Biological Event *Type:* adverse reaction to biologics – compound administered in diet *Secondary Effects*: resulted in interference with study results *Species*: mice
Summary of Event:	Animals (40) were fed a special western diet containing dexamethasone and within 14 days of administration, all animals were either found dead or moribund (immediately euthanized). The animals were monitored at least twice daily by laboratory staff, and the diet adversely affected both experimental and control animals. The laboratory terminated the use of the diet.
Action taken by PI:	The Principal Investigator (PI) self-reported the serious adverse event to the IACUC through the online protocol system in accordance with IACUC policy. The PI further discussed the event with the Attending Veterinarian and provided information to the Office of Animal Welfare. The dexamethasone dose used in the diet formulation was based on a published dose and stated to be well tolerated. The dose was listed in the approved animal use protocol.
Actions Taken to Prevent Future Occurrence of the Serious Adverse Event:	The laboratory collected blood and tissue samples from the moribund animals to measure plasma concentrations and liver toxicity. Future reformulations of the diet will contain lower amounts of dexamethasone. The PI will modify the animal use protocol and obtain approval prior to initiating the administration of the newly modified diet.
Action Taken by IACUC:	At the next convened monthly meeting, the IACUC reviewed the Serious Adverse Report describing the event and the information gathered by the Office of Animal Welfare. The Committee determined that the actions taken by the laboratory were appropriate and adequate. The PI responded to the follow up correspondence from the IACUC. The IACUC felt that the PI responded appropriately and no further action was deemed necessary.

Decision/Resolution:	The IACUC considered the incident resolved.
Federal Funding:	R01 AI152477
Notification of Final Disposition:	☒IO ☒OLAW
Institutional Official: Dr. Melur K. Ramasubramanian	(b) (6) Date: March 7, 2023

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, March 8, 2023 11:03 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: UVA's Serious Adverse Event Report and Preliminary Notification

Good morning (b) (6)

Thank you for sending us this final report for case A3245-4U 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 4:10 PM
To: Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; McCoy, Devora (NIH/OD) [E] <devora.mccoy@nih.gov>
Cc: (b) (6)
Subject: [EXTERNAL] UVA's Serious Adverse Event Report and Preliminary Notification

To whom it may concern: Please find attached UVA's Serious Adverse Event report (see attached preliminary notification).

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

(b) (6)

(b) (6)

[redacted]

A3245-4U

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, January 26, 2023 1:39 PM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: preliminary notification - UVA (Assurance A3245-01); 2022-U

Good afternoon (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 **A3245-4U**, 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: (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: (b) (6)
Subject: [EXTERNAL] preliminary notification - UVA (Assurance A3245-01); 2022-U

Dear OLAW Division of Compliance Oversight,

This is to provide preliminary notification that the University of Virginia IACUC (PHS Assurance #A3245-01) has recognized a serious adverse event involving mice. The UVA tracking number is 2022-U.

Based on preliminary findings, the event was an *unanticipated inadvertent incident* that led to a decline in well-being of a group of animals. The issue is under investigation and review by the IACUC but *does not* appear to be a compliance issue. We will send a separate serious adverse event report once resolved. Should you have any questions or concerns prior to receiving our final report, please do not hesitate to contact me.

Sincerely,
(b) (6)

(b) (6)

[redacted]