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 9, 2022

Re: Animal Welfare Assurance
#A3245-01 (OLAW Case 4K]

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 February 14, 2022 letter reporting an adverse event within the animal care and use program at the University of Virginia, Charlottesville. According to the information provided, OLAW understands that mice were fed a special western diet containing dexamethasone and, within 14 days of administration, all animals were either found dead or moribund. Moribund mice were immediately euthanized. The diet was used as indicated in an IACUC-approved protocol and the animals were monitored twice daily. The dexamethasone diet formulation was based on a published dose which was reported to be well tolerated. The laboratory discontinued the diet and notified the IACUC of the adverse event. The mice involved in this incident were supported by NIH funding.

Corrective and preventive measures included collection of blood and tissue samples from the moribund animals to measure plasma dexamethasone concentrations and liver toxicity. The diet will be reformulated to contain a lower concentration of dexamethasone. The principal investigator will modify the animal use protocol and obtain IACUC approval prior to administration of the modified diet.

OLAW appreciates the consideration of this matter by the University of Virginia, Charlottesville which was consistent with the philosophy of institutional self-regulation. Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate this incident and prevent recurrence. However, in future reports, please include the approximate number of animals affected.

We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

Robyn M. Engel -S

Digitally signed by Robyn M. Engel -S
Date: 2022.03.10 07:40:06 -05'00'

Robyn M. Engel, DVM
Animal Welfare Program Specialist
Office of Laboratory Animal Welfare

cc: IACUC Chair

3245 - 4K

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. This document is a summary of the event, actions taken, and final resolution. The issue was *not* deemed a compliance issue by the IACUC. Due to the rapid reporting and resolution of the unanticipated serious adverse event, a preliminary report was not submitted.

UVA Case #: 2021-V

Adverse Event Classification:	*Scope*: Contained, Inadvertent Event *Sub-Category*: Biological Event *Type:* adverse reaction to biologics – an administered compound in diet *Secondary Effects*: resulted in interference with study results *Species*: mice
Summary of Event:	Animals were fed a special western diet containing dexamethasone and within 14 days of administration, all animals were either found dead or moribund and immediately euthanized. The animals were being monitored at least twice daily and the diet adversely affected both experimental and control animals. The laboratory ended 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 where it was stated that this dose was 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. The laboratory will reformulate the custom diet to contain a lower amount 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 HL141425

Notification of Final Disposition:	☒IO ☒OLAW
Institutional Official: Dr. Melur K. Ramasubramanian	(b) (6) Date: February 14, 2022

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, February 14, 2022 10:09 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Serious Adverse Event Report 2021-W and 2021-X

Thank you for these reports. We will send responses soon.
Axel Wolff

From: (b) (6)
Sent: Monday, February 14, 2022 9:54 AM
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] Serious Adverse Event Report 2021-W and 2021-X

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:

Attached are two adverse event reports from our IACUC. These are 2021-W and 2021-X.

A preliminary report was not sent on these due to the rapid turnaround.

Appropriate corrective action has been taken and the IACUC has determined that this matter is now resolved to their satisfaction.

Thanks,

(b) (6)