



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, Maryland 20892-6910
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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 4L)

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 a tree shrew on a behavior study was given free access to 4% citric acid water as approved in the protocol. The animal was found dead after seven days on the citric acid water. Food and water consumption of animals on study is monitored every 24 hours by the research laboratory. If a large decrease in water consumption or weight is noted, then the animal is removed from study and provided free access to fresh water. However, necropsy findings indicated that the cause of death was likely water deprivation. The tree shrew involved in this incident was supported by NIH funding.

Corrective and preventive measures included decreasing the amount of citric acid in the water from 4% to 3%, which is within the range indicated in the protocol. The principal investigator also agreed to modify the protocol to include more robust monitoring procedures. Animals will be weighed daily for the first week they receive citric acid water and three days a week thereafter. Any animal experiencing weight loss of 10% or more will prompt offering regular water for several hours on the day weight loss is detected. If the animal is placed back on citric acid water, daily weight monitoring will resume.

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. 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 07:39:26 -05'00'

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

cc: IACUC Chair
Dr. Robert M. Gibbens, USDA, APHIS, Animal Care

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 an animal 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 serious adverse 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-X

Adverse Event Classification:	<i>Scope:</i> Contained, Inadvertent Event <i>Sub-Category:</i> Biological Event <i>Type:</i> adverse reaction to biologics – an administered compound in drinking water <i>Secondary Effects:</i> resulting in interference with study results <i>Species:</i> tree shrew
Summary of Event:	The animal was on a behavioral study involving free access to 4% citric acid water. The animal had been on citric acid water previously and had been on regular water for about two months. After seven days of being back on the 4% citric acid water, the animal was found dead. Animals on citric acid water are monitored every 24 hours during training days by the research laboratory. If a large decrease in water consumption or weight is noted, then the animal is removed from study and provided free access to fresh water. According to the necropsy performed by the Attending Veterinarian, the absence of body fat and ketones in the urine lead to the conclusion that the cause of death was likely water deprivation.
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.
Actions Taken to Prevent Future Occurrence of the Serious Adverse Event:	The laboratory will reduce the concentration of citric acid in the water from 4% to 3%. The revised concentration is within the range approved in the animal use protocol. The laboratory previously used 2% citric acid and found it to be ineffective in motivating the animals. Upon receipt of the follow up correspondence from the IACUC, the PI agreed to the modified monitoring regimen. The PI will modify the animal use protocol as needed prior to modifying monitoring procedures.

<p>Action Taken by IACUC:</p>	<p>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.</p> <p>In consultation with the Attending Veterinarian, the IACUC sent the following recommended changes to the monitoring plan: animals should be weighed daily for the first week on citric acid water. If no weigh loss is noted during the first week, then the weigh monitoring can be reduced to monitoring three days a week and each week thereafter while on citric acid water. Any animal experiencing weight loss of 10% should prompt offering regular water for several hours on the day the weight loss is detected. When the animal is placed back onto citric acid water, then monitoring resumes. The PI responded to the follow up correspondence from the IACUC and acknowledged the modified monitoring plan and will proceed with protocol modifications as needed. The IACUC felt that the PI responded appropriately and no further action was deemed necessary.</p>
<p>Decision/Resolution:</p>	<p>The IACUC considered the incident resolved.</p>
<p>Federal Funding:</p>	<p>1U01NS122040</p>
<p>Notification of Final Disposition:</p>	<p><input checked="" type="checkbox"/>IO <input checked="" type="checkbox"/>OLAW</p>
<p>Institutional Official: Dr. Melur K. Ramasubramanian</p>	<p style="text-align: right;">(b) (6)</p> <p>Date: February 14, 2022</p>

Wolff, Axel (NIH/OD) [E]

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

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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,

[REDACTED] (b) (6)