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

October 26, 2021

Re: Animal Welfare Assurance
A3347-01 [OLAW Case 3E)

Dr. Emmanuel Giannelis,
Vice Provost for Life Sciences
Cornell University
(b) (4) Day Hall
Ithaca, NY 14850

Dear Dr. Giannelis,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your September 9, 2021 letter reporting an adverse event at the Cornell University. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the Cornell University Animal Care and Use Committee (ACUC) determined that an adverse event occurred with respect to: one mouse that was found dead. The final report states a homozygous uricase-deficient mouse was found dead and the cause was determined to be due to insufficient allopurinol and improper pH of the drinking water containing allopurinol. It is understood that the research lab prepared the drinking water and adhered to the SOP for preparation. It was determined that pH meter was not functioning properly. Per email communications, it is understood the error with the pH meter resulted in allopurinol precipitating out creating an insufficient concentration. It has since been recalibrated and the pH of the drinking water can now be measured accurately.

The lab will now calibrate the pH meter more frequently to prevent future recurrence. Also, aluminum foil is now used to protect the bottle from light. It is stated that since these corrective actions were taken, there have been no more mortalities and breeding has been successful.

It is understood this research is supported by PHS funds. Based on its assessment of this explanation, OLAW understands that the Cornell University has implemented appropriate measures to correct and prevent recurrences of these problems and is now compliant with provisions of the PHS Policy.

We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,
Jacquelyn T. Tubbs -S
Digitally signed by Jacquelyn T. Tubbs -S
Date: 2021.10.26 14:06:53 -04'00'

Jacquelyn Tubbs, DVM, DACLAM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact

## Walker, Keri (NIH/OD) [E]

**From:** Tubbs, Jai (NIH/OD) [E]
**Sent:** Friday, October 22, 2021 3:13 PM
**To:** Walker, Keri (NIH/OD) [E]
**Subject:** FW: Follow up questions to final report dates September 9th

**Follow Up Flag:** Follow up
**Flag Status:** Flagged

Hi Keri,

Please file this email with case 3347-3E. It provides additional information included in my final response.

Thank you,

J. Tubbs

**From:** [redacted] (b) (6)
**Sent:** Thursday, October 7, 2021 2:14 PM
**To:** Tubbs, Jai (NIH/OD) [E] <jacquelyn.tubbs@nih.gov>
**Subject:** RE: Follow up questions to final report dates September 9th

Hi Dr. Tubbs,

Thank you for reviewing our final report dated September 9, 2021 describing an adverse event where a mouse was found dead due to insufficient allopurinol and improper pH of the drinking water. Cornell has reached out to the researcher regarding your follow-up questions and received the following responses.

Q: Who (research or husbandry staff) prepared the drinking water and the allopurinol concentration?

A: The drinking water was prepared by the research staff.

Q: Was the pH of the drinking water prepared as described (in the protocol or SOP) and still resulted in an improper pH or did staff members not adhere to directions, which resulted in the improper pH in the drinking water?

A: The research lab adhered to the SOP but it was determined that there was something wrong with the pH meter, which they didn't realize at that time. The pH meter has been recalibrated and the pH of the drinking water can now be measured correctly. The lab will calibrate the pH meter more frequently (e.g., before each batch is prepared) to prevent recurrence of this issue.

Q: Was the concentration prepared as described in the protocol or SOP and was still determined to be an insufficient concentration or was the allopurinol not prepared as described and resulted in an insufficient concentration?

A: The research lab adhered to the SOP. The solubility of allopurinol is pH-dependent, thus, the drug would gradually precipitate out if the pH is not high enough. The problem regarding the pH meter mentioned above resulted in the allopurinol precipitating out creating an insufficient concentration. With the recalibration of the pH meter, this issue has been resolved as well.

Please let me know if you have any other questions.

All the best,
(b) (6)

(b) (6)

**From:** Tubbs, Jai (NIH/OD) [E]
**Sent:** Tuesday, September 28, 2021 1:46 PM
**To:** (b) (6)
**Subject:** Follow up questions to final report dates September 9th

Hello,

I am reviewing the final report dated September 9, 2021 describing an adverse event where a mouse was found dead. It is understood that insufficient allopurinol and improper pH resulted in animal death. However, I'm unclear on who (research or husbandry staff) prepared the drinking water and the allopurinol concentration? Please clarify. Also, was the pH of the drinking water prepared as described (in the protocol or SOP) and still resulted in an improper pH? Or did staff members not adhere to directions, which resulted in the improper pH in the drinking water?

Regarding the allopurinol, was the concentration prepared as described in the protocol or SOP and was still determined to be an insufficient concentration? Or was the allopurinol not prepared as described and resulted in an insufficient concentration? Please let me know when you can and thank you for your assistance.

Kind Regards,

Jacquelyn Tubbs, DVM, DACLAM
Animal Welfare Program Specialist
Division of Compliance Oversight

A3347-3E

Cornell University
Office of
Research Integrity and Assurance

395 Pine Tree Road, Suite 320
Ithaca, NY 14850
Phone: 607-255-2214
Fax: 607-255-0758
Email: iacuc@cornell.edu
www.oria.cornell.edu

September 9, 2021

Axel Wolff, MS, DVM, DACLAM
Deputy Director, Office of Laboratory Animal Welfare
National Institutes of Health
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, MD 20892

Animal Welfare Assurance Number: D16-00225 (A3347-01) Cornell University – Ithaca
PHS Grant or Contract Number: NIH R21EB027843

Dear Dr. Wolff:

As Institutional Official for Cornell University's animal care and use program, I am reporting an adverse event involving one mouse that occurred under our General Assurance. This issue was reported to the IACUC at the August 19, 2021 meeting, and the IACUC agreed that the corrective actions taken were appropriate.

**Explanation of the situation:**

One homozygous uricase-deficient mouse was found dead.

**Action taken by the institution:**

The cause of death was determined to be insufficient allopurinol and improper pH of the drinking water containing allopurinol. The pH value of the drinking water was adjusted to 8.5 and the final allopurinol concentration was increased to 90 mg/L. Aluminum foil is now used to protect the bottle from light, which may slow down the deterioration rate. Since these actions were taken, there have been no more mortalities and breeding has continued successfully.

If you have any questions concerning this adverse event that occurred under our General Assurance, please contact [redacted] (b) (6)

Sincerely,

[redacted] (b) (6)

Emmanuel Giannelis
Vice President for Research and Innovation

cc: [redacted] (b) (6) [redacted] (b) (6)
AAALAC International

## Wolff, Axel (NIH/OD) [E]

**From:** OLAW Division of Compliance Oversight (NIH/OD)
**Sent:** Friday, September 17, 2021 7:34 AM
**To:** (b) (6)
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)
**Subject:** RE: Cornell University Report of Noncompliance

Thank you for this report. We will send a response soon.
Axel Wolff

**From:** (b) (6)
**Sent:** Wednesday, September 15, 2021 2:29 PM
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
**Cc:** (b) (6) Office of the Vice President for Research and Innovation <vp_research@cornell.edu> (b) (6)
**Subject:** Cornell University Report of Noncompliance

Dear Dr. Wolff,

Please see the attached report from Cornell University's Vice President for Research and Innovation, Dr. Emmanuel Giannelis, describing an adverse event that occurred under our General Assurance. Please let me know if you have any questions or concerns.

Sincerely,
(b) (6)

(b) (6)