



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

May 31, 2021

Re: Animal Welfare Assurance
A3431-01 [OLAW Case 9N]

Dr. Lisa Muto
Executive Dean for Administration
Harvard Medical School
25 Shattuck Street, Gordon Hall – (b) (4)
Boston, MA 02115

Dear Dr. Muto,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 21, 2022 letter reporting a serious deviation from the provisions of the *Guide for the Care and Use of Laboratory Animals* at Harvard Medical School, following up on an initial report on February 15, 2022. According to the information provided, OLAW understands that 1256 frogs were negatively impacted, with numerous animals dying (including 143 on an NIH grant) or requiring euthanasia, due to contaminated water. A deionized water tank had been incorrectly connected and allowed contaminants to enter the animals' water causing tissue damage and despite remediation efforts, morbidity/mortality occurred.

In addition to the immediate emergency measures taken, the corrective actions consisted of flushing and developing a standard operating procedure for the reverse osmosis system, installing a resistivity meter and resin traps, and marking the ports on the tank. The laboratory will continue to monitor and treat affected frogs.

Based on its assessment of this explanation, OLAW understands that measures are underway to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the institution to comply with the PHS Policy on Humane Care and Use of Laboratory Animals.

Sincerely,

(b) (6)

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

cc: IACUC Chair



HARVARD MEDICAL SCHOOL

LISA M. MUTO, Ph.D.
EXECUTIVE DEAN FOR ADMINISTRATION
HARVARD MEDICAL SCHOOL
25 SHATTUCK STREET, SUITE 408
BOSTON, MA 02115

March 21, 2022

Brent Morse, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

FINAL REPORT

RE: Non-Compliance Report: Assurance: **A3431-01**
Harvard Medical Area Standing Committee on Animals (HMA IACUC)
Species: *Xenopus laevis* **Grant:** 5R01HL098316-08

Dear Dr. Morse,

This letter serves as a final report on an adverse event that was preliminarily reported to OLAW by the Harvard Medical Area Standing Committee on Animals (HMA IACUC) on February 15, 2022.

On February 9, 2022, six ponds undergoing water changes were observed to have resin in the fresh water coming from the RO system. The source of the resin was determined to be from a deionized water (DI) tank that was recently changed for use in the system that was connected via the incorrect port. This caused the contents of the tank, including sodium bisulfite, to be pushed into the system. Affected frogs showing tissue damage were subsequently euthanized. The reverse osmosis DI (RODI) system, including the reservoir, could not be used until it was fully flushed and serviced by technicians who were dispatched to assist as soon as the issue was determined. The ponds were cleaned and filled with city water and treated with sodium thiosulfate, granulated carbon, and the probiotic KoiZyme before frogs were moved from temporary buckets back into these ponds. Frogs were observed in these ponds for three hours on the day of this event. The next morning, a number of the frogs in the impacted ponds were found dead or unhealthy and these were subsequently euthanized. One hundred forty-three (143) of the affected frogs (1256 in total) were partially covered by NIH funding, 5R01HL098316-08.

The lab will continue monitoring and treatment of the exposed frogs. To prevent this from occurring again, the lab is creating a comprehensive SOP for operating the RODI system, installing a resistivity meter that will alert the lab members to any issues wherein they can intervene in the water system if the resistivity registers below 1,000,000 ohms-cm. They are also installing resin traps between the DI tanks and reservoir, and will contact the vendor to provide coverings that will differentiate ports on any DI tanks to be delivered to the aquatics facility. The research group has also agreed to the Committee's stipulation that no new externally-sourced frogs be imported to the facility until the resistivity meter and resin traps have been installed.

The Committee appreciated the lab's ongoing communication with the veterinary staff and members of the Office of the IACUC to identify the cause of this adverse event. The Committee is satisfied with the

corrective actions mentioned above and considers this incident to be resolved. Please let us know if any additional information is required at this time.

Sincerely,

(b) (6)

Lisa M. Muto, PhD

Executive Dean for Administration

HMA Institutional Animal Care & Use Committee: Institutional Official

CC: **Gerald B. Pier, PhD**

Chairman, Harvard Medical Area Standing Committee on Animals

Brian F. Corning, DVM, DACLAM

Executive Director of the Harvard Center for Comparative Medicine, Harvard Medical School:
Attending Veterinarian

(b) (6)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, March 23, 2022 7:18 AM
To: HMS-IACUC
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Final Report. 02/09/2022

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

Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: HMS-IACUC <iacuc@hms.harvard.edu>
Sent: Monday, March 21, 2022 12:03 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: [EXTERNAL] Final Report. 02/09/2022

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and are confident the content is safe.

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, February 18, 2022 7:48 AM
To: HMS-IACUC
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Preliminary Report

Thank you for this preliminary report, (b) (6). We will open a new case file and look forward to receiving the final report from the IO after the IACUC has completed its investigation.

Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: HMS-IACUC <iacuc@hms.harvard.edu>
Sent: Tuesday, February 15, 2022 2:13 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: [EXTERNAL] Preliminary Report

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and are confident the content is safe.

Dear Drs. Morse & Wolff,

The Harvard Medical Area Standing Committee on Animals (HMA IACUC) (D16-00270 (A3431-01)) would like to preliminarily report an adverse event that was brought to the attention of the Office of the IACUC. The adverse event was self-reported by the Research Operations Manager overseeing an aquatics satellite housing facility in which 6 ponds that were rinsing for water changes were observed to have resin in the fresh frog water coming from the reverse osmosis system. The source of the resin was determined to be from a DI tank that was recently swapped out on the system and was connected via the incorrect port, causing it to push the contents of the tank into the system. Filter bags were immediately put around incoming water into the ponds to prevent the resin from entering the ponds. Sodium sulfite was also detected, prompting carbon to be put into each of the filter bags. Water from surrounding ponds that had not yet been drained was siphoned into affected ponds. Buckets were salted and frogs were rinsed with siphoned water and transferred to the prepared buckets or empty acrylic tanks filled with RODI water from a building RODI line. Affected frogs showing tissue damage were subsequently euthanized. Because the RODI system, including the reservoir, could not be used until it was fully flushed and serviced by technicians dispatched to assist as soon as the issue was determined, ponds were cleaned and filled with city water and treated with sodium thiosulfate, granulated carbon, and the probiotic KoiZyme before frogs were moved from the buckets back into these ponds. Frogs were observed in these ponds for 3 hours. The next morning, a number of the frogs in the impacted ponds were found dead. The total mortality amounted to 143 *Xenopus laevis* under NIH grant HL098316.

The Research Operations Manager, along with the principal investigators maintaining this aquatics satellite, veterinary staff, and the company responsible for maintaining and servicing the RODI system have been in discussions regarding remediation efforts, including continued monitoring for the exposed frogs, creating a comprehensive SOP for operating the RODI system, researching a resistivity meter that could alert for any issues to

divert or stop the system if the resistivity registers below 1,000,000 ohms-cm, and capping the improper ports on DI tanks.

We will send a final report providing further details once all the corrective actions have been implemented.

Sincerely,

(b) (6)

