



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

June 2, 2022

Re: Animal Welfare Assurance  
A3114-01 [OLAW Case 4T]

Dr. Rebecca Cunningham  
Vice President for Research and  
Institutional Official  
University of Michigan  
(b) (4) Victor Vaughan Building  
1111 Catherine Street  
Ann Arbor, MI 48109-2054

Dear Dr. Cunningham,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your May 13, 2022 letter reporting 4 unrelated incidents of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals within the animal care and use program at the University of Michigan. According to the information provided, OLAW understands that: Incident 1. A laboratory member did not maintain complete and accurate records of animal care and use activities. Incident 2. Approximately 46 mice were euthanized using expired pentobarbital. Incident 3. IACUC inspectors observed the reuse of a needle across multiple animals and insufficient observation of animals before surgery to ensure complete loss of pedal reflex. Incident 4. Seven mice administered tamoxifen were not maintained in accordance with university policy. A risk assessment determined that personnel safety was not affected. The animals involved in these incidents were supported by NIH funding.

Corrective and preventive measures included: Incident 1. The principal investigator's (PI's) animal care and use program was placed on probation. The PI and all animal handlers were required to retake an online training module regarding animal care and use. The PI is also required to be physically present for all animal activities to ensure appropriate oversight. The laboratory will be subject to enhanced oversight by the IACUC, Attending Veterinarian (AV), and quality assurance specialist. Finally, the PI must submit a corrective action plan to the IACUC including steps to mitigate the potential for future occurrences. Incident 2. The laboratory will review all relevant policies and guidance documents related to the dates of expiration and storage processes for anesthetics, analgesics, and other dilutions. Incident 3. Retraining occurred during the inspection and will continue. Retraining will include a review of all documents related to the preparation for and conduct of surgery, post-operative care, and monitoring. Incident 4. The PI must submit a corrective action plan to include mitigation steps, acknowledgement of the seriousness of adhering to safety measures for hazardous substances, and acknowledgement of the risks of improperly handling hazards to personnel and the environment. In addition, the PI and all laboratory members were retrained on the use of hazards.

Incidents 2 and 4 have occurred in the University of Michigan's animal care and use program previously and will be addressed through program-wide education and retraining.

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OLAW appreciates the consideration of these matters by the University of Michigan 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 these incidents and prevent recurrence. However, in future reports please indicate the species and approximate number of animals involved in each incident. This information was missing for incidents 1 and 3.

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

Sincerely,

Robyn M. Engel -S

Digitally signed by Robyn M. Engel  
-S  
Date: 2022.06.02 10:18:35 -04'00'

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

cc: IACUC contact



# INSTITUTIONAL ANIMAL CARE & USE COMMITTEE

UNIVERSITY OF MICHIGAN

A3114-4T

May 13, 2022

Brent C. Morse, DVM, DACLAM  
Director, Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
RKL1, Suite 360, MSC 7982  
6705 Rockledge Drive  
Bethesda, MD 20892-7982

Dear Dr. Morse:

The University of Michigan, in accordance with Assurance D16-00072 and PHS Policy IV.F.3., provides this report of non-compliance. The below incidents occurred within a relatively short time span. The details of each incident are provided below:

## Incident 1

A lab member did not adhere to the institutional policies regarding the animal care and use of laboratory animals. Specifically, the individual did not maintain complete and accurate records of animal care and use activities. The research is funded through NIH, but the funds used to support this activity were negligible. Accordingly, the NIH funding component was not notified of the situation.

1. The IACUC discussed this matter on February 21, 2022. An additional prior report of concern was considered during the deliberation.
2. The following corrective actions were required:
  - a. The PI's animal care and use program was placed on probation until further notice.
  - b. The PI and all individuals listed as animal handlers on the IACUC approved protocol were required to retake the Orientation to Animal Care and Use online module.
  - c. The PI is required to be physically present for all animal activities occurring in the vivarium to ensure appropriate oversight. Including:
    - i. In-person observation of all animal activities occurring in the vivarium applies to all animal handlers on the PI's protocol (note: additional training may be required for you to gain access to the vivarium).
    - ii. The duration is for at least one month and is dependent on presentation of the below described corrective action plan; and
    - iii. The PI is required to sign all relevant records and forms upon completion of animal activity to ensure adherence to guidelines, regulation, and/or policies.
  - d. The following meetings are required and must include the PI and all animal users working with animals in the PIs lab:
    - i. A meeting with the IACUC Chair and the Attending Veterinarian.

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- ii. Monthly meetings with an ACUO-QA Specialist and a representative from ULAM-Husbandry.
- e. For the duration of the probation, the PI is required to submit weekly reports to the IACUC on the status of his research program. The reports must include:
  - i. The animal activities (procedures) that were conducted during the prior week.
  - ii. The clinical status of these animals (e.g., any required treatment or euthanasia, complications and/or unexpected outcomes) including details that ensure the IACUC understands how the animals were monitored and cared for during the post-procedure period.
  - iii. The action(s) taken and/or treatments given to animals.
  - iv. How ULAM veterinary staff (whether consultation occurred, outcome, etc.) were involved; and
  - v. With the names of the lab staff involved in each procedure listed.
- f. The PI must submit a corrective action plan (CAP) that includes the steps to be taken to mitigate the potential for future occurrences. It must be developed and presented to the IACUC.
  - i. This corrective action plan must be developed for all animal users in the PI's laboratory and must include a checklist for ensuring compliance with applicable IACUC policies, guidelines, and SOPs, adherence to the IACUC approved protocol, and the training and mentoring of new and current staff.
  - ii. This corrective action plan must also be used as a training module in lab for current and future animal users.

## Incident 2

Approximately 46 mice were euthanized using expired pentobarbital (Fatal Plus). The research is funded through NIH, but the funds used to support this activity were negligible. Accordingly, the NIH funding component was not notified of the situation.

1. The IACUC discussed this matter on March 7, 2022.
2. The PI submitted a corrective action plan, which the IACUC reviewed and accepted, that included a lab-wide review of all relevant policies and guidance documents related to the date(s) of expiration and storage processes for anesthetics and analgesics and other dilutions. No further corrective actions were implemented by the IACUC.

## Incident 3

Although animals were not harmed, IACUC inspectors observed the reuse of a needle across multiple animals (to administer anesthetic prior to the non-survival surgery) and insufficient observation of animals before surgery to ensure complete loss of pedal reflex. The research is funded through NIH, but the funds used to support this activity were negligible. Accordingly, the NIH funding component was not notified of the situation.

1. This matter was discussed by the IACUC on March 21, 2022.
2. Re-training occurred during the inspection, and follow-up conversations also are planned (as detailed below).
3. Based on the IACUC discussion, and to mitigate the potential for future reoccurrences, the IACUC required the following corrective actions:
  - Re-training via conversations with a faculty veterinarian and all animal handlers.
  - To mitigate the potential for future reoccurrences, additional re-training must be required:

1. Prepare a list of all documents related to the preparation for and conduct of surgery and post-operative care and monitoring,
2. Review these documents with all individuals listed as animal handlers on the IACUC protocol(s), and
3. Submit, to the IACUC, the list of the documents that were reviewed and a signed attestation that each member reviewed and understood each document.

#### Incident 4

Seven (7) mice administered tamoxifen were not maintained in accordance with University of Michigan policy. The University of Michigan's Environmental Health and Safety Office conducted a risk assessment and determined that no personnel safety was affected. The research is funded through NIH, but the funds used to support this activity were negligible. Accordingly, the NIH funding component was not notified of the situation.

1. The IACUC discussed this matter on April 4, 2022.
2. The IACUC requires the following corrective actions:
  - a. The PI must submit a corrective action plan (CAP) to the IACUC for review. The CAP should include:
    - i. The steps to be taken to mitigate the potential for future occurrences and outline appropriate practices and oversight the PI will take.
    - ii. Acknowledgment of the seriousness of adhering to safety measures when handling and using hazardous materials; and
    - iii. Acknowledgment of the risks associated with the improper handling of hazards, not only to personnel but also to the environment (due to improper disposal of hazardous waste).
  - b. The PI and all associated lab members were required to be retrained on the use of hazards.

The IACUC determined incidents #'s 1 and 3 to be isolated events specific to these labs, and not programmatic in nature. Incidents #'s 2 and 4 have occurred in our program previously and will be addressed through program-wide education and re-training.

The University of Michigan is committed to protecting the welfare of animals used in research and appreciates the guidance and assistance provided by OLAW in this regard. Should you have any questions regarding this report, please contact (b) (6)

Sincerely,

(b) (6)

Rebecca Cunningham, IO and Vice President for Research

(b) (6)

William Greer, Assistant Vice President for Research, and  
Director of the Animal Care and Use Office

Cc: AAALAC International  
IACUC Chair  
Attending Veterinarian

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

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Monday, May 16, 2022 8:40 AM  
**To:** (b) (6)  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: Report for D16-00072

Thank you for this report, (b) (6) We will send a response soon.  
Axel Wolff

**From:** (b) (6)  
**Sent:** Monday, May 16, 2022 8:28 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>  
**Cc:** accredit@aaalac.org; (b) (6)  
**Subject:** [EXTERNAL] Report for D16-00072  
**Importance:** High

Dear Dr. Morse,

Attached please find a report from The University of Michigan's IACUC, assurance # D16-00072.

Please let me know if you have any problems accessing the attachment.

Thank you,

(b) (6)