



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
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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) 402-7065

October 2, 2019

Re: Animal Welfare Assurance
A3291-01 [OLAW Case 3J]

Mr. Joshua Murphy
Chief Legal Officer
Mayo Foundation
200 First Street, S.W.
Rochester, MN 55905

Dear Mr. Murphy,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your September 30, 2019 letter reporting five instances of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Mayo Clinic. Several of the problems were identified during an AAALAC, International site visit and according to the information provided, OLAW understands the following about the incidents and the corresponding corrective actions:

- 1) Three laboratories failed to use sterile technique during rodent survival surgery and failed to provide analgesia as described in the protocol.

Corrective actions: The laboratory staff members were retrained in performing aseptic surgery and how to administer analgesia. The laboratories were directed to develop standard operating procedures (SOP) for surgery training and compliance and these SOPs have been reviewed and approved by the Institutional Animal Care and Use Committee (IACUC). The laboratories have been placed on enhanced post-approval monitoring. An institutional training course in aseptic rodent surgery was developed and the rodent surgery policy was revised.

- 2) One laboratory was not adhering to the humane endpoints regarding tumor size.

Corrective actions: The staff was retrained, SOPs were requested by the IACUC, and the laboratory was placed on enhanced post-approval monitoring. The tumor endpoint policy was revised.

- 3) A satellite zebrafish facility did not have a health status monitoring process and was not being adequately monitored by the IACUC.

Corrective actions: The IACUC counseled the investigators on expectations and documentation, established a health monitoring program, and will rewrite the satellite housing facility policy. The IACUC and post-approval monitors will closely track compliance in this area.

- 4) Neonatal mice were being euthanized by an inappropriate method. The laboratory did not have an effective method to train and bring new members on board.

Corrective actions: The laboratory was given sample documents on onboarding and training and the laboratory will develop SOPs. The animal use privileges for the individual responsible were revoked. The IACUC and post-approval monitors will verify that each laboratory has established appropriate SOPs to onboard new laboratory staff and to ensure adequate training.

5) Retro-orbital bleeding was conducted in mice without anesthesia.

Corrective actions: The animal use privileges for the two individuals responsible were suspended and they were required to undergo retraining. One individual left animal research and the other one was placed under enhanced oversight.

Based on its assessment of these explanations, OLW understands that measures have been implemented in each situation to correct and prevent recurrence of the problem. OLAW concurs with the actions taken by the institution to comply with the PHS Policy. Please remember to indicate whether a noncompliant incident is PHS or NSF supported and provide the relevant grant number(s) if so. Also, note that the PHS Policy requires all individuals conducting animal activities to be trained and assessed for proficiency prior to actually working with animals. Should any further noncompliance be identified by the IACUC or post-approval monitors during the period of enhanced oversight, please promptly report to OLAW. Thank you for keeping OLAW apprised on these matters.

Sincerely,

 (b) (6)

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

cc: IACUC Chair



Institutional Animal Care and Use Committee

200 First Street SW
Rochester, MN 55905

(b) (6)

September 30, 2019

Axel Wolff, M.S., D.V.M.
Director, Division of Compliance
Oversight Office of Laboratory Animal
Welfare Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, MD 20817

Dear Dr. Wolff:

The Mayo Clinic, in accordance with Assurance number D16-00187 (A3291-01) and PHS Policy IV.F.3 provides this report of serious deviations from the *Guide for the Care and Use of Laboratory Animals*. These deviations were found during the AAALAC, Int. site visit, or were reported from Department of Comparative Medicine (DCM) personnel. The IACUC has formed and assigned task forces, consisting of IACUC members, veterinarians, and administrators, to investigate the facts and root causes of each case thoroughly. The IACUC has been reviewing these cases at the last three IACUC meetings and has completed the review process and determinations of corrective actions. The cases are summarized below:

The AAALAC site visitors discovered three laboratories that were not using sterile technique during rodent survival surgery and were not administering analgesia as described in their protocols. The personnel in each of these laboratories were given hands on training by veterinarians from DCM in the correct procedures to perform aseptic surgery and the correct way to administer analgesia. The laboratories have been requested to develop improved standard operation procedures (SOPs) for surgery training and compliance with approved protocols and regulatory guidelines. The SOPs have been submitted, reviewed and approved by IACUC. These laboratories have been placed on enhanced monitoring and will be followed by the post approval monitoring (PAM) personnel to ensure continued compliance.

The AAALAC site visitors discovered a laboratory that was not adhering to humane endpoints relating to tumor size. The personnel in these labs were retrained by veterinarians from DCM and the laboratory has been placed on enhanced monitoring. Improved laboratory SOP has been requested and will be reviewed by the IACUC.

The AAALAC site visitors discovered that the satellite zebrafish facility lacked a health status monitoring process and sufficient oversight by the IACUC. The IACUC has had meetings with the investigators using the zebrafish facility to discuss expectations, required documentation, set up a health monitoring program and will be rewriting the satellite housing facility policy to ensure expectations are documented in a format that all investigators can access. The IACUC will review the policy as soon as it has been submitted, and the IACUC and PAM personnel will be continuing to review improvement and compliance of the facility very closely.

The IACUC received a report from DCM personnel of an inappropriate method of euthanasia

being used on neonatal mice. The IACUC investigated and determined that the laboratory does not have an adequate onboarding and training process for their new members. The IACUC has provided sample documents that can assist in formalizing the onboarding and training process for the laboratory. The IACUC will review the SOPs once they have been submitted. The IACUC voted unanimously that the individual who performed the euthanasia would not be allowed to work with research animals at Mayo Clinic anymore and that the lab would be placed under enhanced monitoring.

The IACUC received a report from a laboratory member that fellow lab members were performing retro-orbital bleeding of mice without using anesthesia. The IACUC removed access to the animal facilities for the personnel involved and performed an investigation. The two individuals were required to go through hands-on retraining and take additional course work in regulatory compliance and animal pain and distress from the AALAS Learning Library. One of the two individuals has left animal research and the other will be placed on enhanced monitoring.

We regret these incidents in our animal program. In addition to the actions that have been taken to the individual laboratories as described above, we have reviewed our animal program and have revised the rodent tumor endpoint policy and rodent surgery policy for clarity and specificity. DCM has created a training course in aseptic rodent surgery that will be used initially as an on-demand course, but eventually will become a required part of the Mayo Clinic animal use training curriculum. We feel that the addition of the two PAM specialists that started in August and September will significantly assist Mayo investigators in remaining compliant with regulations. IACUC and PAM specialist will continue to evaluate and verify that each laboratory has established appropriate SOP to onboard new laboratory personnel and to provide robust training for animal procedures, including but not limited to rodent survival surgeries. Please feel free to contact the IACUC Chair, Dr. Hirohito Kita, at (b) (6) with any additional questions or suggestions.

Respectfully,

DocuSigned by:

(b) (6)

Joshua B. Murphy

Mayo Clinic

Institutional Official and Corporate Secretary

Cc: Hirohito Kita, M.D., Chair, IACUC
Thomas Meier, D.V.M., Attending Veterinarian,

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