



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) 402-7065

June 5, 2019

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

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 May 30, 2019 letter providing the tenth update under an enhanced reporting schedule for the Mayo Clinic to allow this Office to assess the steps being taken to prevent rodent deaths due to lack of food/water. According to the information provided, OLAW understands the following:

- 1) Training of investigators is continuing.
- 2) The Training Specialist has been brought on board and will train and monitor skills of the animal care staff. Efforts are underway to hire a post-approval monitor.
- 3) The Institutional Animal Care and Use Committee (IACUC) addressed the previously reported incident (A3291-3F) of delayed euthanasia of a mouse, unapproved satellite housing, inadequate cage cleaning schedule, and failure to record temperature/humidity. The individual responsible had their workload evaluated, protocol contents will be reviewed by laboratory staff, an animal monitoring standard operating procedure (SOP) was developed, an emergency contact SOP was developed, staff will monitor all animals in the Healthspan Assessment Laboratory twice daily, a daily animal room monitoring log will be maintained, ongoing training of laboratory staff will be conducted regarding all animal activities, a training log will be maintained, new staff will be monitored and mentored, all laboratory staff has completed required training, and some staff will regularly attend the animal users meeting. The IACUC has approved the laboratory's procedures for bringing new staff on board, has placed the laboratory on enhanced oversight, and has accepted the laboratory's corrective actions. (Note that this information will be placed into file A3291-3F and that case is now closed.)
- 4) No serious noncompliance or adverse events have occurred during the previous month.
- 5) The Mayo Clinic Management Engineering & Internal Consulting Department (ME&IC) will examine a variety of components of the husbandry program and will provide advice for improvement of procedures.
- 6) SOPs have been developed for the Healthspan Assessment Laboratory to ensure appropriate oversight.

OLAW concurs with all of the actions underway to improve the Mayo Clinic's animal care and use program. We look forward to receiving the assessment of the ME&IC, any personnel updates, and any other new initiatives in the next report due **July 1, 2019**. 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
507-284-2906

May 30, 2019

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

Dear Dr. Wolff:

The Mayo Clinic, Assurance number D16-00187 (A3291-01), provides this status report due June 1, 2019, as a response to the enhanced reporting request from OLAW to monitor the success of corrective actions outlined in previous communications from Mayo Clinic.

Our progress on the specific action items during the past month is as follows:

1. Update on ongoing training

- We continued providing face-to-face training to investigators. The Institutional Animal Care and Use Committee (IACUC) Chair and Coordinator provided didactic training to the investigators and laboratory staff of the Orthopedic Surgery Program on May 20, 2019.

2. Enhanced oversight provided by additional staff

- A Training Specialist was hired in mid-May to train and monitor skills of current and future DCM staff. This position will ensure consistent and continuous training and evaluation of DCM staff skills.
- The IACUC is accepting applications for a Post Approval Monitoring (PAM) position. Several interview sessions for the candidates have been scheduled for mid-June.

3. Any new or ongoing food and water issues

- The IACUC invited the investigator involved with OLAW Case A3291-3F to the May 22, 2019 IACUC meeting. The investigator presented a corrective action plan for his laboratory personnel and discussed IACUC concerns regarding his laboratory personnel. The plan consists of the following:
 - The individual involved with the non-compliance has had their workload reviewed and monitored by her principal investigators
 - All current IACUC protocols in the laboratory and new protocols will be presented and discussed by the staff responsible for the study in the laboratory meetings.
 - An SOP has been developed to monitor any animals from the laboratory being studied in the Healthspan Assessment Laboratory.
 - An SOP has been developed to check whether there are any animals from the laboratory remaining in the Healthspan Assessment Laboratory. The SOP describes the person to contact in case of an emergency or if daytime staff is on holiday and during holidays. This SOP has been added to the Healthspan Laboratory SOP folder, located in the Healthspan Assessment Laboratory.
 - All of the staff working with animals will be responsible for monitoring the Healthspan Assessment Laboratory on a rotational basis.

- The Healthspan Assessment Laboratory will be checked twice a day for any animals from our laboratory. The monitoring will occur in the morning and at the end of the day.
- Daily monitoring of the room will be recorded and signed in a log book. The log book will contain columns that must be ticked by the monitor for bedding, water, and food. The timing of the animals residing in the Healthspan Assessment room will also be recorded.
- Training for any laboratory procedure will be conducted by senior laboratory staff. They will be responsible for training any new members or current staff about drug administration, blood sampling, observation of animal's health and well-being, their cages, food, and water supply.
- There is a log book for all the laboratory staff members and for any temporary and new staff that contains all the training and skillsets for each member of staff. For any new procedure, a start and end date of the training will be recorded in the log book. A review of the training will be monitored by one of the personnel in charge of the training every time the procedure will be conducted for a period of time not less than 1 month. New personnel will be monitored closely until training has been completed.
- Temporary and new personnel will always be monitored closely by experienced laboratory personnel and they will not be allowed to conduct any procedure independently. Procedures, such as drug administration and blood sampling, will be conducted by two members of staff. The training period will be ended once the experienced staff member considers the trainee fit to perform the procedure. Temporary staff will always be accompanied by another experienced member of staff when dealing with animals, even after their training has been completed.
- The online training and DCM facility orientation has been completed by all members of the laboratory.
- At least one of the staff members will attend the Quarterly Animal Users meetings to ensure the laboratory is up to date with the current animal facility affairs.
- This laboratory is fully committed to implement these changes and to prevent any future non-compliance incidents.
- IACUC reviewed this information and approved the lab's approach to onboarding, housing/husbandry SOP's and involvement of senior laboratory members in training and oversight of newer lab members.
- IACUC will also require monthly reporting for at least 6 months from the laboratory with summaries of laboratory activities and the inclusion of their daily log sheets for oversight of the Healthspan Assessment Laboratory.
- IACUC feels that the investigator is now fully involved and will take all necessary measures to prevent any reoccurrence. We will monitor the progress on an ongoing-basis through the monthly report and by visiting the laboratory if necessary.

4. Any serious noncompliance or adverse events should still be reported promptly and independently of the report

- None have occurred since the last report.

5. Additional measures taken

- The IACUC and DCM have engaged the services of the Mayo Clinic Management Engineering & Internal Consulting (ME&IC) Department. ME&IC uses management engineering methodologies and advanced project management approaches to study and solve the issues in the husbandry program using a systems approach. The consultant has been evaluating the following items and recommendations will be generated based on his findings from the program evaluation:
 - Training
 - Roles and responsibilities/staffing to work load model
 - Value stream mapping/process flow
 - Equipment and supplies (cost benefit)
 - Near miss and death data
 - SWAT analysis
 - GAP analysis

- The Healthspan Assessment Laboratory created a series of SOPs for investigators using the area and for Healthspan Personnel to ensure the area has proper oversight.

We believe that our animal program and quality of animal-based research is improving. We continue to make changes and will make adjustments, if necessary, and look for ways to improve our program. 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,
(b) (6)



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) 402-7065

May 9, 2019

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

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 May 6, 2019 response to my April 15, 2019 request for additional information regarding several serious deviations from the provisions of the *Guide for the Care and Use of Laboratory Animals* at the Mayo Clinic. According to the information provided, OLAW understands the following:

- 1) The investigator is developing the corrective action plan and will present this to the Institutional Animal Care and Use Committee (IACUC) on May 22, 2019. The information requested by the IACUC includes information on:
 - Who is responsible for reviewing workload, satellite/new protocol procedures
 - Which standard operating procedures (SOP) will be developed by the Principal Investigator (PI) and which by Healthspan Assessment Laboratory program, and frequency of review
 - SOP drafts
 - Who will perform laboratory monitoring
 - What will be monitored
 - What documentation will be maintained
 - Who will perform training on laboratory procedures, which procedures. Relevant documentation is to be submitted to the IACUC
 - How new staff is brought on board, how this is documented
 - How new staff is trained and monitored for proficiency
- 2) The study in question is not PHS/NSF funded.
- 3) The housing area had been approved as a satellite facility but only up to 72 hours for animal holding.
- 4) The IACUC met with the PI and staff to outline the concerns and request the corrective action plan.
- 5) The laboratory has been placed under enhanced post-approval monitoring.

- 6) The IACUC has addressed the SOPs to be followed by investigators using the Healthspan laboratory; the IACUC will address how new staff is trained and monitored and this will involve the post-approval monitor to be hired shortly.

Based on its assessment of these explanations, OLAW has a better understanding of the steps being taken by the IACUC to address the immediate noncompliance and the programmatic issue. OLAW concurs with these actions and looks forward to receiving the corrective action plan summary which will be discussed at this month's IACUC meeting. Thank you for keeping OLAW apprised on this matter.

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
507-284-2906

May 6, 2019

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

Dear Dr. Wolff:

The Mayo Clinic, Assurance number D16-00187 (A3291-01), provides this additional information due May 6, 2019, regarding the situation where the investigator failed to euthanize a mouse for three weeks after reaching a humane endpoint and being notified by veterinarians and animal care specialists to do so. In addition, mice were housed in a satellite housing location for three weeks without prior approval, cages were not changed weekly and temperature and humidity were not recorded.

The additional information requested by OLAW:

- 1) **Provide a summary of the corrective action plan developed by the investigator and indicate whether this was approved by the IACUC:** The investigator is working on the corrective action plan for his laboratory. He will present the final version to the IACUC on May 22, 2019 when he attends the IACUC meeting to discuss the plan. IACUC has asked him to focus on the following items
 - Clarify who will be responsible for reviews of workload, satellite lab protocol procedures and new protocol procedures and indicate how the reviews will be performed.
 - Clarify which SOPs are going to be developed by the PI and which SOPs are developed by the Healthspan Assessment Laboratory program and the frequency in which they will be reviewed.
 - Provide the penultimate draft of SOPs to the IACUC by noon May 20th for review by the full committee meeting on May 22nd.
 - Provide the details of who (name and qualifications) will perform the lab monitoring.
 - Clarify what will be monitored, how often, and how the results will be documented.
 - Clarify if there is a log to complete and document laboratory monitoring.
 - Clarify who will be performing the training for laboratory procedures and on which laboratory procedures. Once training is completed, submit the documentation of training to IACUC.
 - Describe the process for on-boarding of new personnel into the lab and explain how this is documented.
 - Provide the content of on-boarding training and clarify whether new personnel will be monitored closely by or working together with experienced laboratory personnel and, if so, how long.
- 2) **Indicate whether the study in question was PHS/NSF supported and provide the grant number(s) if so:** The study in question is not PHS/NSF funded.

- 3) **Indicate whether the housing area was approved as a satellite facility:** The housing area was approved as a satellite housing facility for 72 hours. It was not approved to house animals for three weeks.
- 4) **Indicate whether the investigator met with the IACUC and whether additional action items were required:** The IACUC Chair and members met with the investigator and his laboratory personnel on April 2nd, explained the major concerns by the committee, and coached them to develop corrective action plans. The investigator is attending an IACUC meeting on May 22, 2019 to discuss and finalize the corrective action plan developed by the investigator.
- 5) **Indicate whether the laboratory was placed under enhanced post-approval monitoring:** Yes, the laboratory has been placed under enhanced post-approval monitoring.
- 6) **Indicate whether any additional programmatic changes were implemented to prevent a similar situation in another laboratory:** The incident revealed two potential gags in our animal program; 1) utilization of SOPs in the Healthspan Laboratory and 2) training of inexperienced laboratory personnel in a research laboratory. In response to the request by IACUC, the Healthspan Laboratory area which contains behavioral equipment and a CLAMS unit has developed SOPs for all investigators who wish to use the area. The SOPs clearly detail the responsibilities of the investigators using the area, and these SOPs have been approved by the IACUC. We will also develop a strategy to monitor the onboarding process in research laboratories in conjunction with a new Post Approval Monitoring (PAM) personnel who will be hired this summer.

We will provide a summary to OLAW after the May 22, 2019 IACUC meeting once the plans by the investigator have been finalized and approved. 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,
(b) (6)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, May 7, 2019 7:13 AM
To: IACUC
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Report from Mayo Clinic (D16-00187)

Thank you for this update. I will send a response soon.

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

From: IACUC <iacuc@mayo.edu>
Sent: Monday, May 6, 2019 5:18 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: Report from Mayo Clinic (D16-00187)

Good afternoon,

Please find attached the report from Mayo Clinic's Institutional Animal Care and Use Committee (IACUC) (D16-00187) regarding OLAW Case A3291-3F. Thank you.

Institutional Animal Care and Use Committee (IACUC) | Administrative Services - Research | (b) (6)
(b) (6) | Fax: (b) (6) | iacuc@mayo.edu
Mayo Clinic | 200 First Street SW | Rochester, MN 55905 | www.mayoclinic.org



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) 402-7065

April 15, 2019

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

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 March 28, 2019 letter reporting several serious deviations from the provisions of the *Guide for the Care and Use of Laboratory Animals* at the Mayo Clinic. According to the information provided, OLAW understands that an investigator failed to euthanize a mouse for three weeks after reaching the humane endpoint and after having been notified by the veterinarians and animal care specialists. In addition, mice were housed in a satellite housing location for three weeks without prior approval, cages were not changed weekly, and temperature/humidity were not recorded.

The corrective actions consisted of Institutional Animal Care and Use Committee (IACUC) members counseling the investigator and having the investigator develop a preventive action plan.

In order for OLAW to have a complete understanding of the facts involved in this case, please provide the following additional information:

- 1) Provide a summary of the corrective action plan developed by the investigator and indicate whether this was approved by the IACUC.
- 2) Indicate whether the study in question was PHS/NSF supported and provide the grant number(s) if so.
- 3) Indicate whether the housing area was approved as a satellite facility.
- 4) Indicate whether the investigator met with the IACUC and whether additional action items were required.
- 5) Indicate whether the laboratory was placed under enhanced post-approval monitoring.
- 6) Indicate whether any additional programmatic changes were implemented to prevent a similar situation in another laboratory.

Please provide the requested information by **May 6, 2019**. Feel free to contact me should you have any questions.

Page 2 – Mr. Murphy
April 15, 2019
OLAW Case A3291-3F

Sincerely,

(b) (6)

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

cc: IACUC Chair



New case
A3291-3F

Institutional Animal Care and Use Committee

200 First Street SW
Rochester, MN 55905
507-284-2906

March 28, 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 provides of a serious deviation from the *Guide for the Care and Use of Laboratory Animals* regarding inadequate husbandry of rodents and failure to euthanize an animal that had reached experimental endpoints.

On March 13, 2019, the Institutional Animal Care and Use Committee (IACUC) reviewed a self-report from a laboratory member indicating that the lab:

- Neglected to euthanize a mouse that had reached humane endpoint criteria as requested by the animal care specialists and Veterinarians for three weeks after the first notification;
- Housed mice in a satellite housing location for three weeks without prior approval;
- Neglected to perform cage changes on a weekly basis; and
- Neglected to keep a record of the temperature and humidity of the room while animals were present.

A subcommittee of the IACUC will attend a laboratory meeting of the researcher's to discuss the seriousness of these situations, offer counseling to develop strategies to prevent reoccurrence of these activities and discuss corrective action. The investigator will be required to create a detailed plan discussing the steps the lab will take to prevent reoccurrence of non-compliance and then the investigator will be required to attend an IACUC meeting to discuss their plan with the Full Committee.

We regret this incident in our animal program. Mayo Clinic is committed to protecting the welfare of animals used in research. Please feel free to contact the (b) (6) at (b) (6) if any additional concerns remain.

Respectfully,

DocuSigned by:
(b) (6)
DE3CAE8CF1C0481...
Joshua B. Murphy
Mayo Clinic
Institutional Official and Corporate Secretary

cc: Hirohito Kita, M.D., Chair, IACUC

(b) (6)



Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, April 10, 2019 8:59 AM
To: IACUC; OLAW Division of Compliance Oversight (NIH/OD)
Cc: Kita, Hirohito, M.D.; (b) (6)
Subject: RE: Incident Reports from Mayo Clinic - D16-00187

Thank you for providing these reports. We will send official responses soon.

Best regards, Brent Morse

Brent C. Morse, DVM, DACLAM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

Please note that this message and any of its attachments are intended for the named recipient(s) only and may contain confidential, protected or privileged information that should not be distributed to unauthorized individuals. If you have received this message in error, please contact the sender.

From: IACUC [mailto:iacuc@mayo.edu]
Sent: Monday, April 01, 2019 12:56 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Kita, Hirohito, M.D. <kita.hirohito@mayo.edu>; (b) (6)
(b) (6)
Subject: Incident Reports from Mayo Clinic - D16-00187
Importance: High

Good Afternoon,

Please see the attached incident reports from Mayo Clinic's Institutional Animal Care and Use Committee (IACUC) D16-00187. Thank you!

Institutional Animal Care and Use Committee (IACUC) | Administrative Services - Research | (b) (6)
(b) (6) | Fax: (b) (6) | iacuc@mayo.edu
Mayo Clinic | 200 First Street SW | Rochester, MN 55905 | www.mayoclinic.org