



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500 – MSC 6910
Bethesda, Maryland 20892-7982
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

DATE: January 4, 2023

TO: Nina F. Schor, M.D., Ph.D.
Deputy Director for Intramural Research, NIH

FROM: Deputy Director, Office of Laboratory Animal Welfare

SUBJECT: Animal Welfare Investigation (NIEHS 45-22) - Animal Welfare Assurance
A4149-01 [Case 17X]

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your December 29, 2022 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the National Institute of Environmental Health Science, NIH. According to the information provided, OLAW understands that six mice used in an unapproved pilot study experienced weight loss that was greater than what had been approved in the original Animal Study Proposal (ASP), thus exceeding the approved humane endpoint. The mice subsequently regained their normal body weight.

The corrective actions consisted of counseling the Principal Investigator to adhere to the approved endpoints in the ASP and to amend the protocol if changes are necessary. An amendment was submitted and approved by the Animal Care and Use Committee, the veterinary staff will monitor the next cohort of mice, and all animal users were reminded of the requirement to follow the approved ASP.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the institution to comply with the PHS Policy.

Sincerely,

(b) (6)

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

cc: Dr. Richard Wyatt
Dr. Stephen Denny
Dr. Paul Wade

A4149-17X



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

www.nih.gov

December 29, 2022

TO: Brent C. Morse, D.V.M.
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare

FROM: Deputy Director for Intramural Research, NIH

SUBJECT: Animal Welfare Investigations - Assurance D16-00602 (NIEHS 45-22)

This correspondence conveys the results of an animal incident investigation by the NIH National Institute of Environmental Health Sciences (NIEHS) ACUC in accordance with Assurance D16-00602 and PHS Policy IV.F.3. The incident involved a failure of a laboratory to follow the humane endpoint as set in an ACUC-approved mouse study.

The event was first reported to the NIH Office of Animal Care and Use by the NIEHS ACUC Chair on September 23, 2022.

Please contact me or Dr. Stephen Denny, Director, Office of Animal Care and Use, if additional information or clarifications are required.

Nina F. Schor - S	Digitally signed by Nina F. Schor -S Date: 2022.12.29 20:38:53 -05'00'
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Nina F. Schor, M.D., Ph.D.

Attachment

cc: Dr. Wyatt
Dr. Denny
Dr. Wade



DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health
National Institute of
Environmental Health Sciences
P. O. Box 12233
Research Triangle Park, NC 27709
Website: <http://www.niehs.nih.gov>

Date: November 30, 2022

To: Nina Schor, M.D.
Deputy Director for Intramural Research, NIH

From: Paul Wade, Ph.D.
NIEHS Animal Care and Use Committee Chair

Subject: Reportable Incident of Noncompliance with PHS Policy

In accordance with Assurance D16-00602 and PHS Policy IV.F.3., the NIEHS ACUC provides this report of an incident that occurred involving the care and use of animals in biomedical research.

In September 2022 an amendment was submitted to Animal Study Proposal (ASP) 2021-0014 to extend the humane endpoint of body weight loss to 25%. The amendment justification referenced a pilot study in which six mice experienced body weight loss below 80% of baseline and indicated all the mice survived and reached original bodyweight within a week. The primary reviewer noted the statement and reviewed the original ASP, which did not describe a pilot with different humane endpoints.

The ACUC Program Coordinator was notified 9/22/2022 and contacted the lab for clarification on the pilot. The lab provided weight logs and study details from the cohort that began 7/19/2022. The issue was presented to the NIEHS Animal Care and Use Committee (ACUC) at the 9/22/2022 meeting and the Principal Investigator (PI) was notified that the incident was being investigated and the change in endpoint was not approved and that the currently approved humane endpoints must be followed. The PI responded on 9/27/22 to clarify that the amendment was submitted to prevent unnecessary loss of animals in the model and that the study, which has been approved and conducted by the lab for years. The PI clarified that based upon the overall locomotor activity of the mice and their general health indicators, and his extensive experience working with the Veterinary Medicine Section (VMS) on post-surgical care in this model that he determined the mice were not approaching the point needing euthanasia. The PI instructed the post-doc to provide extra supportive care and monitoring, which included twice daily health checks, provision of mash, and glucose supplementation. The PI further indicated that the post-doc should have been instructed to work with the VMS. The lab provided the body weight logs and VMS verified that no animals from the cohort were written up for adverse clinical signs.

The ACUC chair notified the Director of the NIH Office of Animal Care and Use of this incident on Friday, 9/23/22 and the NIEHS Scientific Director on Saturday, 9/24/22. The ACUC discussed the incident at the October 27, 2022 meeting and deliberated over whether the incident was a non-compliance and reportable. It was acknowledged that the amendment to extend the body weight loss endpoint from 20 to 25% is a potential refinement and that the incident did not result in animal deaths. The ASP approved humane endpoint required that the animals be removed at 20% body weight loss and was exceeded. The ACUC concluded that as the endpoint was approached the lab should have contacted VMS so that a veterinarian could notify the ACUC and an amendment could be developed, submitted, reviewed, and approved prior to the animals reaching the endpoint.

The ACUC voted by majority that the incident is reportable to OLAW based upon the OLAW guidance example of reportable situation "conduct of animal-related activities without appropriate IACUC review and approval; failure to adhere to IACUC-approved protocols" by PHS Policy IV.B.7. The ACUC felt that this incident is an opportunity to refine our process of communicating to animal users and ensuring PIs understand their responsibilities and options when changes to the approved ASP are required. The Chair will meet with the PI to remind him of the requirement to follow the ASP endpoints as approved and to review the actions that should be taken if the endpoints need to be

modified. The ACUC requested that a reminder notice be distributed to active animal users at NIEHS. The Comparative Medicine Branch will also review web content to ensure the ACUC policies are clear and prominently displayed. The amendment to extend the body weight loss endpoint was resubmitted to the ACUC and was reviewed and approved by the ACUC at the November 17, 2022 meeting. The lab was instructed to work with the VMS to monitor the next cohort of animals and procedures and VMS will report back to the ACUC.

(b) (6)



Paul Wade
Chair, ACUC, NIEHS, NIH

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, December 30, 2022 11:46 AM
To: Denny, Stephen (NIH/OD) [E]
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: D16-00602 NIH Animal Incident Report (NIEHS 45-22)

Good morning Dr. Denny,

Thank you for sending us this report and we will send an official response soon.

Best,
Devora

Devora McCoy, BS, MBA
Program Analyst
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
301-435-2390

From: Denny, Stephen (NIH/OD) [E] <stephen.denny@nih.gov>
Sent: Friday, December 30, 2022 11:27 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: D16-00602 NIH Animal Incident Report (NIEHS 45-22)

Dear OLAW/DCO,

The attached documents from the NIH Institutional Official and the NIH National Institute for Environmental Health Sciences (NIEHS) ACUC address a failure to implement study endpoint procedures as outlined in an ACUC-approved Animal Study Proposal. The incident was reported to OACU on September 23, 2022.

If you have any questions please contact me via email or at the phone number listed below. Thank you, Steve

STEPHEN DENNY, DVM, MS, DACLAM, DACVPM | Director, Office of Animal Care and Use | NIH Bethesda Campus, Building 31/Room B1C37 |
Phone: (301) 435-2188 | **NIH . . . Turning Discovery Into Health** |