



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

February 10, 2023

Re: Animal Welfare Assurance
A3304-01 [OLAW Case 4A]

Dana Director, Ph.D.
Vice President of Research Administration &
Senior Staff Officer
Oregon Health and Science University
3181 SW Sam Jackson Park Rd.
Portland, OR 97239

Dear Dr. Director,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your February 3, 2023 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Oregon Health and Science University. Your letter supplements the information in a telephone prompt report made on December 23, 2022. According to the information provided, OLAW understands that on October 23 and 24, 2022, lipopolysaccharide (LPS) was administered to six anesthetized mice via direct instillation to the nares to initiate a model of Cystic Fibrosis. While the method of instillation was approved by the Institutional Animal Care and Use Committee (IACUC) for a separate experimental agent, LPS was only approved for delivery via nebulizer to awake animals in their home cages. Two of six animals died unexpectedly two days after the administration. The other four animals were immediately euthanized. The associated activity was PHS funded.

The OHSU IACUC approved a mitigation plan that included submitting to the IACUC for review an amendment that 1) fully described the procedures for administration of LPS to the nares, the doses to be used, and potential side effects the animals might experience, 2) details of a health monitoring plan which included frequency of monitoring for humane endpoints of appearance, behavior, body weight, respiratory activity, hydration status and body temperature, and 3) criteria indicating when veterinarians would be consulted for prognostic examination. Also, the staff member has been retrained on the importance of full knowledge of the procedures approved by the IACUC and the precise execution of those approved procedures. The Principal Investigator has accepted full responsibility for this incident and for ensuring that all staff, trainees, and students involved in animal activities in their laboratory comply with the approved protocols. The collaborating institution has been notified of this noncompliance and was copied on the final report. Any expenditures were minimal, not requiring refunding the grant.

The consideration of this matter by the Oregon Health and Science University was consistent with the philosophy of institutional self-regulation. Similarly, the actions taken to resolve the issue and prevent recurrence were appropriate. We appreciate being informed of this matter and find no cause for further action by this office.

Page 2 – Dr. Director
February 10, 2023
OLAW Case A3304-4A

Sincerely,

Brent C. Morse -S

Digitally signed by Brent C.
Morse -S
Date: 2023.02.12 14:15:06 -05'00'

Brent C. Morse, DVM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC contact
Director, Animal Care & Use program



A 3304-4A

February 3, 2023

Brent Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare (OLAW)
National Institutes of Health
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, MD 20892

OHSU Research & Innovation

(b) (6)

Dana Director, PhD
Vice President of Research
Administration & Senior Staff
Officer

director@ohsu.edu
www.ohsu.edu/research

Mail code: L335
3181 S.W. Sam Jackson Park
Rd.
Portland, OR 97239-3098

Dear Dr. Morse:

The Oregon Health & Science University (OHSU), in accordance with Assurance D16-00195 (A3304-01) and Public Health Service (PHS) Policy IV.F.3., provides this report of a serious noncompliance with the PHS Policy. A preliminary report was submitted to you on December 23, 2022 via a telephone call from (b) (6)

(b) (6)

This incident occurred on October 23 and 24, 2022 when lipopolysaccharide (LPS) was administered to six anesthetized mice via direct instillation to the nares to initiate a model of Cystic Fibrosis, award HL146736. While the method of instillation was approved by the Institutional Animal Care and Use Committee (IACUC) for a separate experimental agent, LPS was only approved for delivery via nebulizer to awake animals in their home cages. The LPS was administered by a research staff member working in the laboratory. The staff member was trained for delivery of experimental substances directly to the nares and through a nebulizer.

Two of six animals died unexpectedly two days after the administration. The other four animals were immediately euthanized. Given that the IACUC had not appropriately reviewed and approved the administration of this agent directly to the nares as performed by the staff member, the OHSU IACUC Leadership Team categorized this incident as a serious noncompliance which resulted in pain and distress to the animals. The IACUC Leadership Team recommended this incident be reported to OLAW by the Institutional Official in accordance with guidance document NOT-OD-05-034.

The OHSU IACUC discussed the incident and approved the investigator's proposed mitigation plan at a convened meeting on January 18, 2023. The plan included submitting to the IACUC for review an amendment that 1) fully described the procedures for administration of LPS to the nares, the doses to be used, and potential side effects the animals might experience, 2) details of a health monitoring plan which included frequency of monitoring for

humane endpoints of appearance, behavior, body weight, respiratory activity, hydration status and body temperature, and 3) criteria indicating when veterinarians would be consulted for prognostic examination. The IACUC approved the protocol amendment on January 25, 2023. Also, the staff member has been retrained on the importance of full knowledge of the procedures approved by the IACUC and the precise execution of those approved procedures. The Principal Investigator has accepted full responsibility for this incident and for ensuring that all staff, trainees, and students involved in animal activities in their laboratory comply with the approved protocols.

This study was conducted in collaboration with Oregon State University, who has been notified of this noncompliance and copied on this final report. We have determined that expenditures were minimal, not requiring refunding the grant.

OHSU 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)
(b) (6)

Thank you for your consideration of this matter.

Sincerely,

(b) (6)

Dana Director, Ph.D.
Vice President of Research Administration & Senior Staff Officer
Institutional Official
Oregon Health & Science University

Cc: Attending Veterinarian
IACUC Chair
Director, Animal Care & Use Program
Oregon State University Office of Integrity

McCoy, Devora (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, February 6, 2023 1:46 PM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: final report of noncompliance

Good afternoon (b) (6)

Thank you for sending us the final report for case A3304-4A and we will send an official response soon.

Best,
Devora

Devora McCoy, BS, MBA ([pronunciation](#))
Program Analyst
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

Phone: 301-435-2390
Email: devora.mccoy@nih.gov

From: (b) (6)
Sent: Monday, February 6, 2023 1:18 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Dana Director <director@ohsu.edu>; (b) (6)
(b) (6)
Subject: [EXTERNAL] final report of noncompliance

Dear Dr. Morse,
Please find attached a final report from Oregon Health & Science University related to a serious non-compliance.
If you have any questions, please feel free to reach out to me directly.
Respectfully,

(b) (6)



Initial Report of Noncompliance

By: BCM

Date: 12/23/2022

Time: 2:57

Name of Person reporting: (b) (6)
Telephone #: (b) (6)
Fax #:
Email:

Name of Institution: Oregon Health Science Univ.
Assurance number: A3304

Did incident involve PHS funded activity? ?
Funding component:
Was funding component contacted (if necessary):

What happened: Unapproved agent administered to 6 mice. Two died, four euthanized.

Species involved: Mice
Personnel involved: researcher
Dates and times: 10/28 - 29/2022
Animal deaths: yes

Projected plan and schedule for correction/prevention (if known):

Projected submission to OLAW of final report from Institutional Official:

< 60 days

OFFICE USE ONLY
Case #