



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500, MSC 6910
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FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

DATE: November 1, 2018

TO: Michael M. Gottesman, M.D.
Deputy Director for Intramural Research, NIH

FROM: Deputy Director, Office of Laboratory Animal Welfare

SUBJECT: Animal Welfare Investigation (#015-18) - Animal Welfare Assurance
A4149-01 [Case 12 P]

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your October 29, 2018 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the National Institute for Dental and Craniofacial Research, NIH, following up on an initial report on October 15, 2018. According to the information provided, OLAW understands that mice on a bone fracture study failed to receive the protocol required post-operative analgesia. The mice did receive a short acting dose of analgesia prior to the procedure.

The corrective actions consisted of requiring the Principal Investigator and staff to attend relevant training at a professional conference, placing the laboratory on a one year probation, having veterinary technicians oversee the provision of analgesia as necessary following the bone fracture, and having the PI submit a memo to the Animal Care and Use Committee (ACUC) stating that approved pain management practices will be used.

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 ACUC to comply with the PHS Policy.

(b) (6)

Axel Wolff, M.S., D.V.M.

cc: Dr. Richard Wyatt
Dr. Stephen Denny
Dr. Mark Hoon



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

www.nih.gov

October 29, 2018

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 A4149-01 (#015-18)

This correspondence conveys the results of an investigation by the National Institute for Dental and Craniofacial Research ACUC, in accordance with Assurance A4149-01 and PHS Policy IV.F.3. The adverse event involved a failure to follow postoperative procedures outlined in an NIDCR ACUC-approved animal study protocol.

The event was first reported to the NIH Office of Animal Care and Use by the NIDCR Attending Veterinarian on October 12, 2018. The details of the ACUC investigation and the corrective actions taken by the animal care program are outlined in the attached memorandum.

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

(b) (6)

Michael M. Gottesman, M.D.

Attachment

cc: Dr. Wyatt
Dr. Hoon
Dr. Denny
Dr. Davidson



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of Dental
and Craniofacial Research
Bethesda, Maryland 20892

To: Michael M. Gottesman, M.D.
Deputy Director for Intramural Research, NIH

From: Mark Hoon, Ph.D.
ACUC Chairperson, NIDCR, NIH

(b) (6)

Date: October 16, 2018

RE: OLAW Reportable Incident

This memo is regarding a reportable incident that occurred within the National Institute of Dental and Craniofacial Research (NIDCR) Animal Care and Use Program (A4149-01). The incident involves mice that were not treated with post-operative analgesia (buprenorphine). The mice had undergone surgery that induced bone fractures (ASP 15-788).

A subcommittee of the ACUC met with the PI, responsible investigators, and the Attending Veterinarian to investigate the incident. In summary, the findings indicated that mice that were used in bone fracture experiments were not treated with post-op analgesia. Only one dose of short acting buprenorphine was given pre-op. No adequate justification was given for not using postop analgesia. Since there was no adequate justification presented to the Committee, pain management regimen is required for mice that have undergone major surgery as outlined in the approved ASP (currently modified to a minimum of two doses of sustained release buprenorphine).

At the July 19, 2018 monthly meeting, the Committee deliberated on the subcommittee report and decided on the following actions:

- Withholding analgesia from mice that have undergone major surgical procedure is a serious violation of approved ASP procedures, PHS policy, and the Guide, potentially subjecting the animals to unnecessary pain and distress, and therefore is OLAW reportable.
- The PI and the responsible animal user should attend a training/webinar on "compassion fatigue," attend a seminar at the upcoming 69th AALAS conference to be held in Baltimore, MD. The Committee asked the APD to identify the appropriate training. Three trainings/courses/workshops were

identified for investigators to review the requirements on alleviating pain/distress, and providing care to animals following established procedures. The recommendations included:

- **“Compassion Fatigue Review” (Webinar)** offered by AALAS at <https://www.labroots.com/webinar/compassion-fatigue-education-engagement-animal-research>.
- AALAS Seminar at AALAS National Meeting (Baltimore; Tuesday October 30, 2018). Seminar titled **“Anesthesia and Analgesia in Rodents, Updates on Rodent Anesthesia and Postoperative Analgesia”**
- **“Monitoring for Humane Endpoints: Developing an Appropriate Strategy”** offered by OLAW at <https://olaw.nih.gov/education/educational-resources/webinar-2018-09-20.htm>

The training must be completed in the next 6 months.

- A one-year probation is instituted in which any future noncompliance within a year will lead to a more serious action including and up to suspension of an animal study.
- Mice that undergo the bone fracture surgery should be provided with SR buprenorphine for as long as the mice require analgesia. The schedule of analgesia and written records after it is provided to the mice, will be supervised/monitored by the VRC veterinary technicians for one year.
- Mice that have undergone bone fracture surgery should be treated with perioperative analgesia until the time the pain from the procedure is known to subside. The duration of treatment can be based on known human requirements with similar injuries; this may mean that one week of analgesia treatment may be required. Mice, as prey animals, tend to mask pain/distress, which would make it difficult to clearly see the magnitude of pain they are experiencing. When it is difficult to determine whether an animal is in pain or not, the best option is to consider whether the condition is painful to humans.
- The PI should reexamine the lab's established pain assessment procedures and align these with veterinary approved pain management practices. The ACUC would like the PI to write a memo to the ACUC describing their commitment to currently accepted animal welfare protocols. The memo to the ACUC should also acknowledge the expectations of the ACUC and indicate how the PI intends to prevent similar incidents from happening in the future.

We appreciate your assistance with this issue and will provide any additional information as requested.

Cc: Dr. Richard Wyatt
Dr. Matt Hoffman
Dr. Stephen Denny
Dr. Lauren Davidson

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, October 31, 2018 1:06 PM
To: Denny, Stephen (NIH/OD) [E]; OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: A4149-01 NIH Adverse Animal Incident Report (NIDCR 015-18)

Thank you for providing this final report Dr. Denny. We will send an official response soon.

Best regards, Brent Morse

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

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From: Denny, Stephen (NIH/OD) [E]
Sent: Wednesday, October 31, 2018 12:49 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: A4149-01 NIH Adverse Animal Incident Report (NIDCR 015-18)

Dear OLAW/DCO,

Final reports from the NIH Institutional Official and the National Institute of Dental and Craniofacial Research ACUC addressing an animal incident reported to this office on October 12th are attached. The incident involved a principal investigator failing to provide postoperative care as described in his NIDCR ACUC-approved animal study proposal.

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

STEPHEN L DENNY, DVM, MS, DACLAM | Acting Director, Office of Animal Care and Use | National Institutes of Health | Bldg 31-Rm B1C37, 9000 Rockville Pike, Bethesda, MD 20982 | Phone: (301) 496-5424 | <http://oacu.od.nih.gov>

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, October 16, 2018 6:48 AM
To: Denny, Stephen (NIH/OD) [E]
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: A4149-01 Reportable Event NIH-NIDCR ACUC (015-18)

Thank you for this preliminary report, Dr. Denny. We will start a new case file and look forward to receiving the final report from the IO after the IACUC has completed its investigation.

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

From: Denny, Stephen (NIH/OD) [E]
Sent: Monday, October 15, 2018 9:08 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: A4149-01 Reportable Event NIH-NIDCR ACUC (015-18)

Dear OLAW/DCO –

On October 12, the Attending Veterinarian for the National Institute of Dental and Craniofacial Research (NIDCR) informed this office of a reportable animal incident involving failure to adhere to IACUC approved protocols; more specifically, the failure to provide appropriate care and post-operative management to mice as outlined in the IACUC approved protocol.

The NIDCR ACUC will perform a full investigation, propose corrective actions, and render a report in the near future. Sincerely, Steve

STEPHEN L DENNY, DVM, MS, DACLAM | Acting Director, NIH Office of Animal Care and Use | Phone: (301) 496-5424