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

September 8, 2020

Re: Animal Welfare Assurance
A3646-01 [OLAW Case 1J]

Dr. Jon Reuter
Assistant Vice Chancellor for Research Integrity and Compliance
University of Colorado – Boulder
3100 Marine Street, UCB 563 (b) (4)
Boulder, CO 80309

Dear Dr. Reuter,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your August 17, 2020 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Colorado Boulder. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the University of Colorado Boulder Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to: failure to adhere to the IACUC-approved protocol. The final report states on July 10, 2020, inspections of surgical records indicated that 0.035ml buprenorphine had been administered to mice. It was determined that buprenorphine was given from a diluted 0.03 mg/ml buprenorphine HCl solution. No additional post-operative analgesia was documented in the surgical records. The analgesic approved in the protocol is buprenorphine SR. It was discovered that for studies utilizing the CCI model at the University of Washington, opioid analgesia cannot be administered because it alters the inflammatory response. The report states the principal investigator (PI) administered one dose of buprenorphine pre-operative to relieve incisional pain. It is further stated that to ensure comparability between data collected from these studies the PI seeks to replicate the protocol previously used for this model at the University of Washington. Also, an amendment was submitted to the protocol to increase the dosing range of buprenorphine SR in addition to following the CU Veterinary Anesthetic and Analgesic Formulary for mice for future studies.

It is noted the study was not supported by PHS funds. Based on its assessment of this explanation, OLAW understands that the University of Colorado Boulder has implemented appropriate measures to correct and prevent recurrences of these problems and is now compliant with provisions of the PHS Policy. We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,

Jacquelyn T. Tubbs -S

Digitally signed by Jacquelyn T. Tubbs -S
Date: 2020.09.08 11:37:23 -04'00'

Jacquelyn T. Tubbs, DVM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact

A3646-1J

University of Colorado Boulder

Jon Reuter, Assistant Vice Chancellor for
Research Integrity and Compliance
3100 Marine St, UCB 563, Office 25
Boulder, CO 80309

jon reuter@colorado.edu

t 303 735-5809

New case

August 17, 2020

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

Dr. Morse,
The University of Colorado Boulder, Assurance No. D16-00388, provides the following reports listed below. Due to COVID-19 and the closure of the University investigative results were delayed. We are sending these reports as all the information has been presented to the IACUC and found to be reportable.

Protocol : 2469 Species: Mice
Funds: DOD EP150033

6/25/20 During inspections it was found the lab was giving a single dose of buprenorphine HCl rfollowing a traumatic brain injury procedure. Buprenorphine was not listed on the protocol. Instead, carprofen was listed as an analgesic, with a dosing strategy of 24 hours for 3 days after surgery. According to records, this was not being done and animals were receiving a single dose of buprenorphine HCl which only lasted for ~ 6 hour. Upon investigation and consults with the lab it was found that Lab staff were not aware that Buprenorphine HCl was not listed in the protocol, nor were they aware that Carprofen was listed. Lab staff had been instructed by previous lab staff/students that a single dose of Buprenorphine HCl lasted for ~24-48 hours.

The improper usage of Buprenorphine HCl has ceased and been rectified with protocol amendments. Lab staff have been retrained and have now switched to using SR Buprenorphine to ensure that post-operative pain is being properly managed. In addition, the current lab staff have reviewed the most up-to-date CU Boulder Veterinary Guidelines for anesthetics and analgesics and the approved protocol.

Protocol: 2582 Species: Mice
Funds: State of Colorado RFP 2019000047

7/10/20 During inspections surgical records indicated that 0.035 mL buprenorphine was administered. Cross-comparison with controlled substance logs and storage safe indicated that this was administered from a diluted 0.03 mg/mL buprenorphine HCl solution. No additional post-op analgesia was noted in the surgical records. The protocol is approved for administration of buprenorphine SR, but not buprenorphine HCl. The single dose of buprenorphine HCl provided only 6-8 hours of analgesia.

In discussion with the principle investigator it was found that for studies using the CCI model at the University of Washington opioid analgesics were unable to be administered because it altered the inflammatory response. The principal investigator had administered one dose of buprenorphine prior to surgery to relieve incisional pain. To ensure comparability between data obtained from these studies the principle investigator seeks to replicate the protocol previously used for this model at the University of Washington. An amendment was submitted to his protocol in addition to following the CU Veterinary Anesthetic and Analgesic Formulary for mice for future studies.

CU Boulder maintains its commitment to the health and welfare of animals used in research. Should you have any questions regarding this report, please contact Christopher A. Lowry, PhD, IACUC Chair at christopher.lowry@colorado.edu or Althea R. Lantron, IACUC Director, at althea.lantron@colorado.edu.

Sincerely,

DocuSigned by:
(b) (6)
4125465D4B0945A...

Jon Reuter, Assistant Vice Chancellor of Research Integrity and Compliance

Cc:
Christopher A. Lowry, IACUC Chair
Althea R. Lantron, Director, IACUC Director
Sara Hashway, Director, Office of Animal Resources

## Morse, Brent (NIH/OD) [E]

**From:** Morse, Brent (NIH/OD) [E]
**Sent:** Wednesday, August 26, 2020 9:31 AM
**To:** mailto:Althea.Lantron@Colorado.EDU
**Subject:** RE: Report of Non-compliance - CU Boulder

Thank you for providing this report Ms. Lantron. 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



**From:** OLAW Division of Assurances (NIH/OD) <olawdoa@od.nih.gov>
**Sent:** Monday, August 24, 2020 4:06 PM
**To:** Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>; Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
**Cc:** OLAW Division of Assurances (NIH/OD) <olawdoa@od.nih.gov>
**Subject:** FW: Report of Non-compliance - CU Boulder

**From:** Althea Lantron <Althea.Lantron@Colorado.EDU>
**Sent:** Monday, August 24, 2020 3:50 PM
**To:** OLAW Division of Assurances (NIH/OD) <olawdoa@od.nih.gov>
**Subject:** Report of Non-compliance - CU Boulder

Dear All,

Attached is the latest report of non-compliance found during inspections.

*Althea R. Lantron*
Director, Institutional Animal Care and Use
University of Colorado - Boulder
2860 Wilderness Pl, (b) (4)
Boulder, CO 80301
Email: althea.lantron@colorado.edu
Phone: (b) (6)

**NOTE**: Due to COVID-19 mitigation efforts, IACUC staff are working remotely at this time. IACUC staff will be monitoring all emails and phone messages during normal business hours while also processing protocols. We appreciate your patience as we adapt to this ongoing situation.