



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

December 10, 2020

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

Dr. Jon Reuter
Assistant Vice Chancellor for Research Integrity and Compliance
University of Colorado – Boulder
3100 Marine Street, UCB 563 Office 25
Boulder, CO 80309

Dear Dr. Reuter,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your November 18, 2020 letter describing three reportable incidents within the animal care and use program at the University of Colorado - Boulder. All three incidents occurred on activities receiving PHS-funding. According to the information provided, OLAW understands that on 9/21/20 a rat incurred two broken femurs while undergoing an approved inescapable shock treatment within a small chamber. The animal was properly monitored throughout the experiment and nothing unusual was noted. The following day, after being unresponsive to treatment for reduced hind-limb mobility, the rat was euthanized and it was discovered both femurs were fractured, presumably as a result of the rat kicking the back of the chamber during the experiment. There was no noncompliance associated with this adverse event.

Corrective and preventive measures include modifying the test chambers and re-training of staff by a PI experienced in the use of the devices and the appropriate placement and restraint of the animals. The Attending Veterinarian will stay in regular contact with the laboratory regarding the success of the above measures in preventing injury.

On 10/14/20 it was determined that a new procedure space had already been in use by a lab for mouse procedures prior to IACUC approval. The procedure space did not have any deficiencies during IACUC inspection, and to correct the noncompliance, the lab submitted amendments to add the space to the appropriate protocols, which were subsequently approved.

On 11/06/20 the dosing of AK-28 (an antagonist at Toll-like receptor 4) was miscalculated to be 10 times the concentration it was intended. Doses are approved in the protocol at no more than 100mg/kg but were delivered at 150mg/kg. As a result, within five minutes of the injections, rats experienced seizures. The supervisor was summoned, and the animals were euthanized immediately. No further doses of AK-28 were administered to animals after this time.

In order to address this issue, the lab will have drug calculations double-checked by a second person to avoid miscalculations, animals will be observed for 15 minutes following injection of AK-28, and the lab has made contact with the company that makes the AK-28 for more information regarding their ongoing studies and if seizures have been observed. If seizures are observed when the injections are administered at the approved doses in future studies, the lab will adjust dosing to achieve lower physiological concentrations.

OLAW believes that the corrective and preventive measures by the University of Colorado - Boulder are consistent with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals for institutional self-monitoring and self-reporting. We appreciate being informed of these matters and find no cause for further action by this office.

Sincerely,

Brent C. Morse -S

Digitally signed by Brent C.

Morse -S

Date: 2020.12.10 13:24:05 -05'00'

Brent C. Morse, DVM

Director

Division of Compliance Oversight

Office of Laboratory Animal Welfare

cc: IACUC contact



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 A3646-12

November 18, 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. Please note that the incident on 9/21/20 was investigated and discussed at a convened IACUC meeting where due to the pandemic and staff not being on sight the Attending Veterinarian (AV) was tasked with following up with the lab to determine how best to prevent the incident from occurring again. The AV was also requested by the IACUC to provide a report at the next convened meeting. The results are as follows:

Protocol: 2565 Species: Rats
Funds: NIDA: DA044980 (R01) & NIDA: DA045952 (R21)

On 9/21/20 a rat underwent an inescapable shock treatment, in which it was exposed to a series of tail-shocks within a small chamber. The animal was monitored throughout the experiment remotely, the experimenters did not note anything unusual or uniquely dangerous during the test. After the animal was removed from the test it was sensitive to touch and showed some minor abrasions on the paws, around the nails. During the post-treatment assessment the experimenter noted the legs were still responsive to touch and were capable of movement. The following day during OAR routine health checks, the animal care technician identified the animal as showing minimal hindlimb movement. After examination by OAR veterinary staff, the animal was given wet food and an injection of analgesic/anti-inflammatory. After minimal improvement was seen in the animal's condition the Attending Veterinarian made the call to euthanize the rat and perform a necropsy. During the necropsy it was discovered both femurs were fractured, presumably as a result of the rat kicking the back of the chamber during the experiment.

This adverse event occurred during an IACUC approved procedure and adhering to the protocol guidelines. In order to address this issue, the lab is making modifications to their test chambers. These modifications include placing padding on the back wall of the test chambers, identifying which removable chamber pieces belong to each box so the components fit appropriately, adding tops to the test chambers to discourage animals from kicking harder in an attempt to escape from the top, and re-training of staff by a PI experienced in the use of the devices and the appropriate placement and restraint of the animals. The lab has also invited the Attending Veterinarian to observe the procedure in the modified test chambers once the next set of experiments have been scheduled. The procedure has been performed since the adverse event was reported in a different set of chambers that belonged to a PI experienced in this procedure. In the trial run on October 29, two out of eight animals run in the experiment had hindlimb swelling. The attending veterinarian examined all animals and treated the two affected animals with an anti-inflammatory, after which the swelling resolved. Since that trial, additional trials have been run without incident. Still, the lab plans to invite the experienced PI to observe future sessions and offer additional suggestions for improvement. The Attending Veterinarian will stay in regular contact with the laboratory regarding the success of the above measures in preventing injury.

Protocol: 2539 & 2618

Species: Mice

Funds: NIH: R01 HL134887, NIH: F32 HL140875, & NIH: R01 AG055822

On 10/14/20 a new procedure space was inspected by an IACUC sub-committee for approval of use on the labs protocols. At the time of the inspection it was found that the lab had already been using the procedure space, prior to IACUC approval.

The use of the space prior to IACUC approval was found to be a serious non-compliance. The procedure space did not have any deficiencies during the inspection and the lab submitted an amendment to add the space to the appropriate protocols which were approved on 10/15/20 and 10/19/20.

Protocol: 2412

Species: Mice and Rats

Funds: NIH R01NS097313

On 11/06/20 the dosing of AK-28 (an antagonist at Toll-like receptor 4) was miscalculated to be 10 times the concentration it was intended. Doses are approved in the protocol at no more than 100mg/kg subcutaneous but were delivered at 150mg/kg subcutaneous. As a result, within five minutes of the injections lab personnel observed the rats experiencing seizures. Upon seeing the first seizure the personnel called her supervisor. The supervisor immediately headed to the facility to assess the situation. Once the supervisor arrived the animals were euthanized immediately. No further doses of AK-28 were administered to animals after this time.

This adverse event was unintentional and due to human error. In order to address this issue, the lab will have drug calculations double-checked by a second person to avoid miscalculations, animals will be observed for 15 minutes following injection of AK-28, and the lab has made contact with the company that makes the AK-28 for more information regarding their ongoing studies and if seizures have been observed. Although it is not expected, if seizures are observed when the injections are administered at the approved doses in future studies, the lab will adjust dosing to achieve lower physiological concentrations.

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)
41261650490545A

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

OLAW Division of Compliance Oversight (NIH/OD)

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, November 19, 2020 1:37 PM
To: IACUC Office
Cc: Althea Lantron; Jon D Reuter; Sara Hashway; Christopher Lowry
Subject: RE: Reportable Incidents

Thank you for providing these reports. 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: IACUC Office <iacucoffice@colorado.edu>
Sent: Thursday, November 19, 2020 10:11 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Althea Lantron <Althea.Lantron@Colorado.EDU>; Jon D Reuter <Jon.Reuter@Colorado.EDU>; Sara Hashway <Sara.Hashway@colorado.edu>; Christopher Lowry <christopher.lowry@colorado.edu>
Subject: Reportable Incidents

Dear OLAW,

Please find attached the final report for the incidents that we have found reportable.

Thank you,

(b) (6)

Be Boulder.



University of Colorado Boulder

Walker, Keri (NIH/OD) [C]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, November 19, 2020 1:44 PM
To: Walker, Keri (NIH/OD) [C]
Subject: FW: Reportable Incidents A3646-1L
Attachments: OLAW Report 2020-1118.pdf

Follow Up Flag: Follow up
Flag Status: Completed

Please open a case file and assign it to Axel. Thanks

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

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University of Colorado **Boulder**