



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) 402-7065

September 12, 2019

Re: Animal Welfare Assurance
A3448-01 [OLAW Case 1B]

Bruce Doll, DDS, Ph.D., MBA
Assistant Vice President for Technology
Research and Innovation
IACUC Institutional Official
Uniformed Services University of the Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814

Dear Dr. Doll,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your September 4, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Uniformed Services University of the Health Sciences, following up on an initial report on April 10, 2019. According to the information provided, OLAW understands that four rats were anesthetized and subjected to an approved procedure consisting of pneumatic air blasts. The rats were given analgesia prior to the blast and were to receive another dose three hours following surgery. In this situation the second dose was given upon recovery from the procedure which was too soon, caused an overdose, and resulted in the deaths of two animals. Also, the rats had been left unattended while recovering from anesthesia.

The corrective actions consisted of amending the protocol to clearly state when the analgesic is to be given and to assess pain and give drugs when needed. Rats will be observed until recovered from anesthesia and a post approval monitoring conducted during the next procedure found all procedures to be compliant.

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: IACUC Chair



UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES

OFFICE OF THE VICE PRESIDENT FOR RESEARCH
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4799
www.usuhs.edu



September 4th 2019

Brent C. Morse, DVM, DACLAM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
RKL1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda MD 20892-7982

Final Incident Report (OLAW Assured Facility Number D16-00285)

Dear Dr. Morse,

This is a final report on an incident at Uniformed Services University of the Health Sciences (USU) OLAW Assured Facility Number D16-00285 (A3448-01) that was initially reported to the Office of Laboratory Animal Welfare (OLAW) on 10 April 2019.

The USU IACUC received information on Wednesday 10 April from one of the Principal Investigator's (PI) staff members concerning an unexpected outcome during a procedure.

A staff member self-reported an adverse event that happened with their protocol on 3 April 2019. Four rats were given two doses of buprenorphine, one prior to an approved injury/surgical procedure and then upon recovery from general anesthesia. Two of the rats were unable to be recovered, but the other two survived. The second dose of buprenorphine SR was given approximately 5 hrs after the first buprenorphine dose. Upon consultation with the veterinarian, that, compounded with the surgical and other stressors applied during the approved protocol, resulted in the unexpected deaths. The PI discovered this was in violation of the protocol, which states that the rats are to receive the dose of Buprenorphine SR 3 hours after surgery and not upon recovery.

The IACUC Chair was notified and appointed a subcommittee to conduct an investigation into the inquiry. The subcommittee reviewed the self-report, the approved protocol and the approved major modification, and then met separately with the Co-Investigator, the PI, and the veterinarian to discuss the incident and procedures described in the protocol.

The IACUC made the following recommendations:

- (a) There was confusion on when to administer buprenorphine. The decision to give sustained release buprenorphine prior to initiation of the first stressful procedure appeared reasonable to the subcommittee and was justified by successful completion of the full protocol by a subsequent

Learning to Care for Those in Harm's Way

Obtained by Rise for Animals. Uploaded 08/24/2020

Retrieved from Animal Research Laboratory Overview (ARLO)

cohort of rats following the revised analgesia procedure. This modification should be included in a revised version of the protocol. The timing of administration of the sustained release buprenorphine dose should be clearly indicated, together with the specific timing and frequency after recovery from anesthesia at which animals will be evaluated using the Pain Assessment Score Sheet to determine if additional post-surgical analgesia is required. It is recommended that rats should be evaluated for additional pain medication at 1 hr after recovery of righting reflexes as the anesthetic is eliminated, and again at about 3 hrs after recovery of righting reflexes, and then at a minimum frequency of twice daily (morning and night; or more frequently) on subsequent post-surgical days until euthanasia on completion of the protocol.

(b) The self-report suggests that the initial cohort of rats was left unattended prior to recovery from anesthesia. It is an IACUC requirement that anesthetized animals be observed during recovery from anesthesia until they have recovered to sternal recumbancy. The PI must ensure that for future cohorts someone is assigned to observe the rats until full recovery from the anesthetic.

(c) A follow-up post-approval monitoring will need to be completed at the next iteration of the procedure by IACUC members.

The PI agreed to all recommendations put forth by the IACUC. A revised protocol was submitted and approved. A team of IACUC members completed a post approval monitoring of the procedure and reported that everything went accordingly.

The IACUC now considers this incident closed.

Sincerely,

(b) (6)

Bruce Doll, DDS, Ph.D., MBA
Assistant Vice President for Technological Research and Innovation
Office of the Vice President for Research
Institutional Official

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, September 11, 2019 12:11 PM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: (b) (6)
Subject: RE: Final Report - USUHS D16-00258

Thank you for providing this final report (b) (6) 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: (b) (6)
Sent: Wednesday, September 11, 2019 9:00 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; DHA NCR Reg Support Mailbox R202 <dha.ncr.reg-support.mbx.r2o2@mail.mil>; USARMY Ft Detrick MEDCOM USAMRMC Other ACURO <usarmy.detrack.medcom-usamrmc.other.acuro@mail.mil>
Cc: (b) (6) Bruce Doll <bruce.doll@usuhs.edu>; (b) (6)
Subject: Final Report - USUHS D16-00258

Good morning Dr. Morse,

Please see the attached final report regarding an unanticipated event from April 2019.

If you require any further information, feel free to contact me.

Thanks,

(b) (6)

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(b) (6)

Prelim.

A3448-1B

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, April 11, 2019 8:56 AM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: USARMY Ft Detrick MEDCOM USAMRMC Other ACURO; (b) (6) Bruce Doll;
(b) (6)
Subject: RE: Preliminary Report - USUHS - D16-00285 (A3448-01) 10April19

Thank you for providing this prompt preliminary report (b) (6) We will open a case file and await further information.

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: (b) (6)
Sent: Wednesday, April 10, 2019 3:38 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: USARMY Ft Detrick MEDCOM USAMRMC Other ACURO <usarmy.detrack.medcom-usamrmc.other.acuro@mail.mil>;
(b) (6) Bruce Doll <bruce.doll@usuhs.edu>; dha.ncr.reg-support.mbx.r2o2@mail.mil;
(b) (6)
Subject: Preliminary Report - USUHS - D16-00285 (A3448-01) 10April19

Dear Dr. Wolff,

Please find the attached initial incident report regarding a rat protocol at the Uniformed Services University. A final report will be submitted by the IO once the investigation has concluded.

Thank you for your review.

(b) (6)

From: iacuc@usuhs.edu [mailto:iacuc@usuhs.edu]

Sent: Wednesday, April 10, 2019 11:24 AM

To: iacuc@usuhs.edu

Cc: (b) (6) iacuc; (b) (6)

Subject: Re: Self Report for SUR-18-065

(b) (6)

Please see the below message from (b) (6) on behalf of the PI, Dr. Thomas (protocol number SUR-18-065, attached).

While (b) (6) is on leave, would you be willing to appoint members to a sub-committee for this event? I spoke with (b) (6) and they both are willing to help and/or sit on the committee. I suggest having (b) (6) on board as well since she has worked closely with the protocol staff.

If all are OK, I will send a preliminary report to OLAW and ACURO today.

Thank you,
(b) (6)

On Wednesday, April 10, 2019 at 8:43:55 AM (b) (6) wrote:

Good Morning,

My name is (b) (6) I write to you on behalf of our PI, Dr. Thomas Davis for protocol SUR-18-065. We would like to self report an event that happened with our protocol that occurred on 3 April 2019.

This was the first day of our new protocol. We perform our procedures on 4 SD rats at a time. The procedures begin with the rats are induced with isoflurane to undergo a pneumatic air blast. The rats then recover and are taken to LAM to undergo a surgical procedure that takes approximately 5 hours that is performed under isoflurane. Under our protocol, based on our previous experiments at NMRC, the rats receive a dose of buprenorphine before the blast and they receive a dose of buprenorphine SR following surgery.

On 3 April, we gave Buprenorphine SR to the rats as they recovered from the procedure. This is in violation of our protocol, which states that the rats are to receive the dose of Buprenorphine SR 3 hours after surgery. Following surgery, three of the four rats showed signs of distress.

These rats were alive and breathing while we were cleaning, approximately 1 hour after surgery and then when we returned to the housing room, one rat was dead, and another stopped breathing. We immediately alerted (b) (6) of the vet staff, who came to assess the rats. We took the rat in distress to the OR in LAM and gave it oxygen and CPR, but the rat died after 10 minutes. Upon returning, we reviewed the anesthesia charts, the pain medicine given, and determined that the rats had likely overdosed on the buprenorphine due to the shorter interval between pain meds. The other two rats recovered and are still alive.

We discussed the case with (b) (6) directed us to give only the Buprenorphine SR at the beginning of our procedures for our next round of rats. The following cohort of 4 tolerated the procedures without complications.

The actions we will take are the following: This self report to the IACUC, we will send in an amendment for our protocol so that we are only giving Buprenorphine SR at the beginning of our procedures and reassess throughout the post operative period and when the Buprenorphine SR wears off if the rats require more analgesia.

Please let us know what further steps we need to take regarding this event and our protocol going forward. Thank you for your time.

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Respectfully,

(b) (6)

A staff member from Dr. Thomas Davis' lab, for protocol SUR-18-065, self-reported an adverse event that happened with their protocol on 3 April 2019. The IACUC was informed on 10 April 2019.

Pneumatic air blast and surgical procedures were performed on four SD rats. Animals were anesthetized with general anesthesia and were given buprenorphine. Upon recovery the rats were given another dose of buprenorphine but were given the dose too soon and as a result two rats died and the other two successfully recovered. The PI discovered this was in violation of the protocol, which states that the rats are to receive the dose of Buprenorphine SR 3 hours after surgery and not upon recovery.

The IACUC and AV are currently working to form a sub-committee for an investigation.



Division of Compliance Oversight

Record of Call for Case # A3448-1B

Date & Time	Message	Initials
8/20/19 10:40	(b) (6) + new A/v called. Final report to be sent soon. They were waiting to observe procedure.	mm