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

January 15, 2020

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

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 January 9, 2020 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 (USUHS).

According to the information provided, this Office understands that the USUHS Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to: the deaths of 8 swine anesthetized during an ocular trauma surgical training lab. Emergency procedures were administered by veterinary staff when the animals began losing vital parameters. The final report states animals were adequately monitored throughout the event and given necessary supportive care. The IACUC formed a subcommittee and 8 individuals were interviewed about various processes such as animal receipt, anesthesia, and surgical procedures. The medical records were inspected, and the study protocol was reviewed. It was determined the adverse event's root cause was directly anesthetic related, but other factors were present. The following findings were discovered during the investigation:

- No animal suffering occurred in these unexpected outcomes, since all animals received appropriate anesthesia, monitoring and supportive care.
- The high dose of induction medications was the significant contributing factor to premature deaths.
- The amount of retrobulbar lidocaine as an analgesic agent per eye was determined to be excessive, although protocol approved.
- Many of the animals experienced heat stress upon receipt from a fully conditioned vehicle.
- A newly formed veterinary team of technicians assisted with anesthesia oversight and not all members were familiar with the location of anesthetic equipment or emergency drugs.
- Animal transfer to training room incurred delays due to elevator access issues.

The IACUC made the following recommendations:

- Have the PI meet with the Attending Veterinarian to prepare a modification to the protocol to adjust the pre-medication regimen and frequency/timing of retrobulbar blocks.
- Ensure each anesthetic drug is given separately and not prepared as a cocktail.

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

Retrieved from Animal Research Laboratory Overview (ARLO)

- Recommend providing adequate acclimation of animals upon future receipts to ensure animals are healthy and not an anesthetic risk.
- Ensure all surgery staff undertake documented training lead by trained veterinary staff to ensure veterinary team is fully familiar with all procedures.
- When possible, conduct all future training events within or nearby designed animal use spaces to reduce overall transport time for anesthetized animals.

The PI agreed to all recommendations put forth by the IACUC and the IACUC now considers this incident closed. Is it noted the protocol under which this event occurred received neither PHS nor NSF funding.

Based on its assessment of this explanation, OLAW understands that the USUHS 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,

(b) (6)

Jacquelyn T. Tubbs, DVM
Veterinary Medical Officer
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact

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

Retrieved from Animal Research Laboratory Overview (ARLO)

A3448-1E

Tubbs, Jai (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
To: IACUC; OLAW Division of Compliance Oversight (NIH/OD); USARMY Ft Detrick MEDCOM USAMRMC Other ACURO; DHA NCR Reg Support Mailbox R2O2
Cc: (b) (6) Bruce Doll
Subject: RE: Preliminary Report - USUHS - D16-00285 (A3448-01) 23 May 2019

Thank you for this final report. An official response will be sent soon.

Kind Regards,

Jacquelyn Tubbs, DVM, DACLAM
Veterinary Medical Officer
Office of Laboratory Animal Welfare
National Institutes of Health

Please note that this message and any of its attachments are intended for the named recipient(s) only and may contain confidential, protected or privileged information that should not be distributed to unauthorized individuals. If you have received this message in error, please contact the sender.

From: IACUC <iacuc@usuhs.edu>
Sent: Friday, January 10, 2020 10:18 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; USARMY Ft Detrick MEDCOM USAMRMC Other ACURO <usarmy.detrick.medcom-usamrmc.other.acuro@mail.mil>; DHA NCR Reg Support Mailbox R2O2 <dha.ncr.reg-support.mbx.r2o2@mail.mil>
Cc: iacuc@usuhs.edu; (b) (6) Bruce Doll <bruce.doll@usuhs.edu>
Subject: Fwd: Preliminary Report - USUHS - D16-00285 (A3448-01) 23 May 2019

Hi Dr. Morse,

Please see the attached final report signed by the Institutional Official. Feel free to contact us if you have any comments or concerns.

Thank you so much,
(b) (6)

--
(b) (6)

Obtained by Rise for Animals. Uploaded 08/24/2020
Retrieved from Animal Research Laboratory Overview (ARLO)

Obtained by Rise for Animals. Uploaded 08/24/2020
Retrieved from Animal Research Laboratory Overview (ARLO)

Morse, Brent (NIH/OD) [E]

From: (b) (6)
Sent: Thursday, January 09, 2020 1:14 PM
To: OLAW Division of Compliance Oversight (NIH/OD)
Cc: iacuc@usuhs.edu
Subject: OLAW Final Report Update; USUHS - D16-00285 (A3448-01) 23 May 2019

Follow Up Flag: Follow up
Flag Status: Flagged

Hi Dr. Morse,

We are waiting on the IO to sign the final report regarding an event in which 8 anesthetized swine died during an ocular trauma course. We will send it to you as soon as we receive the signed copy.

Thank you for your patience,
(b) (6)

--
(b) (6)

Obtained by Rise for Animals. Uploaded 08/24/2020
Retrieved from Animal Research Laboratory Overview (ARLO)

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

09 January 2020

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 D16-00258 (A3448-01)

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 23 May 2019.

The USU IACUC was first notified on Thursday 23 May of an event in which eight fully anesthetized swine died prematurely as part of a two-day annual ocular trauma surgical training laboratory (terminal event). Emergency procedures, including chest compressions and IV epinephrine, were administered by veterinary staff when patients began losing vital parameters. All patients were adequately monitored throughout the event and given necessary intraoperative supportive care (fluids, supplemental heat source, etc). All ocular tissues were utilized for training and no additional animals were needed to complete the training events. The unexpected outcomes were reported promptly to the Attending Veterinarian and the USUHS IACUC. The IACUC subsequently formed a subcommittee to investigate this occurrence. The protocol under which this event occurred received neither PHS nor NSF funding.

A total of eight people were interviewed by the IACUC subcommittee about various processes, including: animal receipt, housing, anesthesia, patient transport, and surgical procedures. Swine medical records were also inspected from this year's event and previous years' iterations. The study protocol was also reviewed. It was determined the adverse event's root cause was directly anesthetic related, but other related factors were present. The following findings were discovered:

1. No animal suffering occurred in these unexpected outcomes, as all animals received

Obtained by Rise for Animals. Uploaded 08/24/2020
Retrieved from Animal Research Laboratory Overview (ARLO)

adequate veterinary anesthesia, proper veterinary monitoring, and supportive care throughout the training events.

2. The most significant contributing factor to the premature deaths was the high dose of induction medications used.
    a. Xylazine does not offer much of the needed sedative effects versus the considerable cardiovascular and respiratory depressive properties.
    b. The use of telazol has also been attributed to anesthetic deaths more frequently than any other type of pre-medication.
    c. The combination of telazol/xylazine causes a marked cardiodepressive effect. Additionally, manipulation of the ocular area can also cause bradycardia and the combination of all three can cause issues.
3. Times of death did not follow any particular pattern, but most animals succumbed within a short period after injection of retrobulbar lidocaine as an analgesic agent. Although approved in the parent protocol, the amounts of retrobulbar lidocaine delivered per eye was excessive. The additional manipulation of the eye with injecting the lidocaine within a shorter time frame combined with the higher than optimal dose of xylazine likely compromised patient cardiovascular parameters greatly.
4. Many of the animals experienced heat stress upon receipt from a fully conditioned vehicle, though this did not specifically correlate with a failure to survive.
5. A newly formed veterinary team of technicians was receiving animals and assisted in the anesthesia oversight of the laboratory. Not all members were familiar with the location of anesthetic equipment or emergency drugs.
6. Patient transfer to the training room incurred delays due to elevator access issues. Although not directly contributory to the events, this is concerning regarding patient supportive care.

<u>The IACUC made the following recommendations:</u>

1. Have the PI meet with the Attending Veterinarian to prepare a modification to the protocol adjusting the pre-medication regimen (removing xylazine completely) and the frequency/timing of the retrobulbar blocks. There are additional options for topical ocular lidocaine than a retrobulbar block and may not even be necessary if bupivacaine is included in the block.
2. Ensure each anesthetic drug is given separately and not prepared as a cocktail. Cocktails complicate the ability to give accurate dosages especially when quicker follow-on doses are needed.
3. Recommend providing adequate acclimation of animals upon future receipts to better ensure animal patients are healthy and are not at additional anesthetic risk.
4. Ensure all surgery staff undertake documented training lead by trained veterinary staff to ensure the veterinary team is fully familiar with all procedures of large animal receipt, quarantine, anesthesia patient preparation (including intubation), and anesthesia equipment.
5. When possible, conduct all future training events within or nearby designed animal use spaces to reduce the overall transport time for anesthetized animals and distance from training space anesthetic support equipment and limit the need for elevator access.

The PI agreed to all recommendations put forth by the IACUC. A modification has been processed and approved by the IACUC to adjust the pre-medication regimen and the frequency/timing of the retrobulbar block. The next two recommendations and the last item have been adopted and implemented as stated. Lastly, all surgery staff have been adequately trained.

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

Retrieved from Animal Research Laboratory Overview (ARLO)

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

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

Retrieved from Animal Research Laboratory Overview (ARLO)