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

August 12, 2021

Re: Animal Welfare Assurance
A3031-01 [OLAW Case 1J]

Dr. Andrew S. Weyrich
Vice President for Research
The University of Utah
(b) (4) Park Building
Salt Lake City, UT 84112

Dear Dr. Weyrich,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your August 3, 2021 letter reporting an adverse event at the University of Utah (U of U). This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the U of U Animal Care and Use Committee (ACUC) determined that an adverse event occurred with respect to: administration of an overdose of ketamine-xylazine to a guinea pig resulting in the death of the animal. The final report states on July 1, 2021, the correct dose of ketamine and xylazine was administered to the animal for ABR/DPOAE hearing test prior to a terminal procedure. Twenty-five minutes after administration, the guinea pig did not seem to be responding to the anesthetic. The lab thought they might have miscalculated the dose and administered an additional dosage for a total of 800mg/kg ketamine and 80mg/kg xylazine, which resulted in the animal expiring.

The event notification form stated the following corrective actions to avoid future recurrence:

- Personnel involved in the ABR/DP procedures received additional anesthesia training from a Clinical Veterinarian on July 9, 2021. The Clinical Veterinarian supervised the entire procedure with hands on training from drug calculation, to injection, to anesthesia state monitoring. It is noted the procedure was successfully performed and the animal recovered uneventfully.

- The lab submitted an amendment to include the specific dosage of ketamine and xylazine in the protocol.

- For future experiments, the lab will have two individual researchers calculate the drug dosage separately and compare the notes to double check accuracy. If the specified dose does not provide proper depth of anesthesia, we will consult the clinical veterinarian for advice on further dosing.

It is understood the committee reviewed the matter and corrective action plan on July 29, 2021 and determined no additional actions were necessary.

It is noted that this project is supported by PHS funds. Based on its assessment of this explanation, OLAW understands that the University of Utah has implemented appropriate measures to correct and prevent recurrences of these problems.

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: 2021.08.12 15:29:19 -04'00'

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

cc: IACUC Contact
Robert M. Gibbens, DVM, Director, Animal Welfare Operations

A3031-15

VICE PRESIDENT FOR RESEARCH
THE UNIVERSITY OF UTAH

August 3, 2021

Brent C. Morse, DVM
Department of Health and Human Services
Rockledge, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

Dear Dr. Morse,

Under provision of IV.F.3 of the Animal Welfare Assurance Policy and as the Institutional Official at the University of Utah (U of U), I am providing OLAW with a full explanation of circumstances in regard to an adverse event.

Name of Institution: University of Utah
Assurance Number: A3031-01

The Principal Investigator notified the IACUC of a potential adverse event via an event notification form concerning the below mentioned protocol on July 6, 2021. The IACUC Director notified the IACUC Chair and the Attending Veterinarian of the potential adverse event on July 6, 2021. Upon discussion with the IACUC Chair, it was determined that this event would be reviewed at the next convened IACUC meeting to be held on July 28, 2021.

The following is a summary of the event as provided by the Principal Investigator:

1. Protocol number: *20-07012*
2. Protocol title: *Magnetic Guidance for Improved Cochlear Implant Insertion*
3. Funding agency: *NIH*
4. Animal species: *Guinea pig*
5. Age of animal(s): *4 months*
6. Number of animals involved in the event: *1*
7. Date(s) that the event occurred: *July 1, 2021*
8. Overview of the adverse event:
   Miscalculated ketamine/xylazine dose for ABR/DPOAE hearing test prior to a terminal procedure scheduled on 07/01/21. At first, we gave a correct dose of 80 mg/kg ketamine 8 mg/kg xylazine for anesthesia, and after waiting for about 25 minutes we noticed the guinea pig did not seem to be responding to the anesthetic. So we mistakenly thought that we might have miscalculated by a factor of 10 and gave an additional dosage for a total of 800 mg/kg ketamine and 80 mg/kg xylazine, which ended up euthanizing the animal.
9. Was there inadvertent pain involved in the adverse event (more than momentary)?: *No*
10. Describe the corrective actions to avoid future problems:
    Personnel involved in the ABR/DP procedures received additional anesthesia training from a Clinical Veterinarian on 7/9. The Clinical Veterinarian supervised the entire procedure with hands on training from drug calculation, to injection, to anesthesia state monitoring. We successfully performed the ABR/DP auditory measurements on the animal under anesthesia and the animal recovered in about 1.5 hour after the drug dosing. We have also submitted an amendment to include the specific dosage of ketamine (40-90 mg/kg)-xylazine (5-13 mg/kg) in the protocol to prevent future adverse events like this from occurring. For any future experiments, we will have two individual researchers calculate the drug dosage separately and compare the notes to double check accuracy. If the specified dose does not provide proper depth of anesthesia, we will consult the clinical veterinarian for advice on further dosing.

August 3, 2021

11. Provide a conclusion: *A member of the research team mistakenly administrated an overdose of ketamine-xylazine to one of the guinea pigs that was to undergo electrophysiologic hearing testing. That team member and others that are working with the guinea pigs under this protocol received additional training by the Clinical Veterinarian. We will be more mindful of the dose of ketamine/xylazine given for anesthesia prior to ABR or other procedures under the IACUC protocol. We will have 2 members of the team check the appropriate dosing and record that value in the laboratory records. If proper depth of anesthesia is not achieved, we will consult the Clinical Veterinarian before proceeding.*

The IACUC, at a convened meeting on July 28, 2021, discussed the details of the event and the corrective actions provided by the Principal Investigator as written above.

The committee determined that this was a serious adverse event due to an unfortunate mistake and that it will be reported to the Office of Laboratory Animal Welfare (OLAW) and to USDA. The committee agreed with the corrective actions as described by the Principal Investigator. No additional action was requested by the committee.

In conclusion, the IACUC determined that this is a serious adverse event that will be reported to OLAW and USDA since it is federally funded. The committee voted unanimously to report the adverse event to OLAW and USDA and agreed with the corrective actions. The Principal Investigator was requested to report this to the agency that is funding this research.

The IACUC Director met with the Institutional Official on August 2, 2021 and determined that the corrective actions provided by the Principal Investigator were adequate and that no further action is required.

Sincerely,

(b) (6)

Andrew Weyrich, Ph.D.
Vice President for Research
Institutional Official

cc. Derek Dosdall, Ph.D.
IACUC Chair

Robert Gibbens, DVM
Director, Animal Welfare Operations
USDA-APHIS-AC

Alton Swennes, DVM, MS, DACLAM
Attending Veterinarian

U of U IACUC Office Files

Morse, Brent (NIH/OD) [E]

From: Morse, Brent (NIH/OD) [E]
Sent: Wednesday, August 4, 2021 10:35 AM
To: (b) (6)
Cc: Andrew S Weyrich; Derek Dosdall; aswennes@ocm.utah.edu; (b) (6)
Subject: RE: 20-07012 OLAW Adverse Event Letter 03AUG21 - University of Utah

Thank you (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

From: (b) (6)
Sent: Tuesday, August 3, 2021 11:13 AM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>; animalcare@usda.gov; robert.m.gibbens@usda.gov
Cc: Andrew S Weyrich <andy.weyrich@utah.edu>; Derek Dosdall <derek.dosdall@utah.edu>; aswennes@ocm.utah.edu; (b) (6)
Subject: 20-07012 OLAW Adverse Event Letter 03AUG21 - University of Utah

Dear Brent Morse and Robert Gibbens,

Please see the attached 20-07012 OLAW Adverse Event Letter 03AUG21 from Dr. Andrew Weyrich. Feel free to contact me if you have any questions.

Thank you,
(b) (6)

(b) (6)

THE UNIVERSITY OF UTAH