DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:
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Home Page: http://grants.nih.gov/grants/olaw/olaw.htm

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Office of Laboratory Animal Welfare
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6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
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February 28, 2017

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

Dr. Yvonne T. Maddox
Vice President for Research and
Institutional Official
Uniformed Services University of the Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20814

Dear Dr. Maddox,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your 14 February, 2017 letter reporting a noncompliance with the PHS Policy on the Humane Care and Use of Laboratory Animals at the Uniformed Services University of the Health Sciences. Your letter supplements information provided in the initial email report from Dr. Cox on December 8, 2016. According to the information provided, OLAW understands that during the afternoon of November 15, 2016 a graduate student collected blood from 17 mice with a hemophilic phenotype. Although silver nitrate was applied to the tail snip area, the student noticed blood in the cage upon rechecking the mice an hour later. Additional silver nitrate was applied. The student did not re-visit the animals. Thirteen mice were found dead the following morning and four mice were moribund and subsequently euthanized. There was blood in the cages. It was not noted if this activity was PHS-funded.

The corrective actions consisted of the IACUC recommending that the graduate student and other lab staff be retrained in blood collection and hemostasis in the hemophilic mice. The PI should also submit a protocol modification indicating that all blood collections will be completed in the morning and specifying the timing and frequency of checking mice after blood collection.

OLAW believes that the corrective and preventive measures put in place by Uniformed Services University of the Health Sciences are consistent with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals for institutional self-monitoring and self-reporting. In future reports please indicate if the activity was PHS-funded. OLAW appreciates being informed of this issue and finds no cause for further action.

Sincerely,

Brent C. Morse, DVM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814-4712

14 February, 2017

Brent C. Morse, DVM, DACLAM
Animal Welfare Program Specialist
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 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 A3448-01) that was initially reported to the Office of Laboratory Animal Welfare (OLAW) on 8 December 2016 and acknowledged by your office on the same date.

On Tuesday, November 15, 2016, around 16:00, a graduate student collected blood from 17 mice housed in 4 cages using a tail snip procedure. This procedure was performed as part of an approved protocol using mice with a hemophilic phenotype, being homozygous for a mutant allele of the Factor VIII clotting factor (so-called "E16" knockout mice). The graduate student was listed among the study personnel on the protocol and had completed USU investigator training and the rodent handling class. After sample collection, silver nitrate was applied to the tail incision sites to promote hemostasis. Around 17:00 the graduate student returned and observed blood on the bedding. Additional silver nitrate was applied to the tail incisions of all the animals that had a tail snip procedure. The graduate student did not re-visit the animals after the re-application of silver nitrate.

On Wednesday, November 16, 2016, around 07:00, a Center for Laboratory Animal Medicine (LAM) technician discovered that thirteen mice from the four cages were dead and four mice were moribund. The moribund animals were immediately euthanized by the (LAM) personnel. On this same day, the Institutional Animal Care and Use Committee (IACUC) chair and IACUC members were given a preliminary briefing on the incident and established a subcommittee to investigate the incident. On Thursday, November 17, 2016, the Institutional Official and her staff were advised of the incident.

On Monday, November 21, 2016, members of the IACUC subcommittee met with the LAM veterinarian overseeing this incident and the primary investigator. Following these meetings the IACUC subcommittee developed the following recommendations:

- The graduate student and other laboratory staff should be retrained, with specific emphasis on blood sampling procedures and on ensuring subsequent hemostasis is achieved in this hemophilic mouse line.

- The PI should submit a minor modification request for the protocol to indicate that all blood collections from hemophilic mice will be completed in the morning to permit monitoring during the day when the LAM is fully staffed. Study personnel will check-in on mice 30 minutes following the completion of each blood collection. If there are signs of hemorrhage (e.g. blood on bedding), steps should be taken to ensure bleeding completely stops. This may include both the re-application of silver nitrate and consulting with a LAM technician or veterinarian (on-duty or on-call). A subsequent check-up after 30 minutes is required whenever there is evidence of bleeding.

- The protocol modification request should be updated to more clearly detail in the Technical Methods section of the protocol the blood collection procedures that are to be employed and the methods to be used to prevent hemorrhage. This modification should also recommend consultation with a LAM technician (on-duty or on-call) in the event of persistent hemorrhage from sampling sites.

The IACUC discussed these recommendations at the scheduled meeting of the IACUC on 18 January 2017 and agreed by unanimous vote to accept the subcommittee recommendations. The proposed retraining of the student and laboratory staff is in progress, and the Principal Investigator has submitted a modification request for the protocol that has been reviewed and approved.

This incident is now considered closed.

Sincerely,

Yvonne T. Maddox, Ph.D.
Vice-President for Research, and Institutional Official

Morse, Brent (NIH/OD) [E]

From: Morse, Brent (NIH/OD) [E]
Sent: Wednesday, February 15, 2017 3:03 PM
To: [redacted]
Cc: [redacted]
Subject: RE: USUHS Final Incident Report (OLAW Assured Facility Number A3448-01)

Thank you for this report. We will send an official response soon.

Regards, Brent Morse

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

From: [redacted]@usuhs.edu]
Sent: Wednesday, February 15, 2017 10:12 AM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Cc: [redacted]@usuhs.edu>
Subject: USUHS Final Incident Report (OLAW Assured Facility Number A3448-01)

Good morning Dr. Morse,

Please find attached the final incident report signed by the Vice President for Research, Dr. Yvonne Maddox.

If you have any questions, please let me know.

Best, [redacted]

[redacted]
Executive Assistant to the
Vice President for Research (VPR)
Uniformed Services University of the Health Sciences (USUHS)
4301 Jones Bridge Road | Bethesda, MD 20814

Office [redacted]
Email [redacted]@usuhs.edu

UNIFORMED SERVICES UNIVERSITY
of the Health Sciences

A3448 - V

Morse, Brent (NIH/OD) [E]

From: Morse, Brent (NIH/OD) [E]
Sent: Thursday, December 08, 2016 2:11 PM
To: 'Brian Cox'
Cc: Megan Ralls; Secondary individu; condary individu
Subject: RE: Initial Report of Incident Re Animal Welfare - Uniformed Services University

Thank you Dr. Cox. We will open a compliance case file and await further information.

Regards, Brent Morse

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

From: Brian Cox [mailto:brian.cox@usuhs.edu]
Sent: Thursday, December 08, 2016 1:20 PM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>
Cc: Secondary individual @usuhs.edu>; Secondary individual @usuhs.edu>; econdary individua @usuhs.edu>
Subject: Initial Report of Incident Re Animal Welfare - Uniformed Services University

Dr. Morse,

I am writing to report a recent incident in the animal care program at Uniformed Services University, Bethesda MD.
At about 0700 on the morning of Wednesday, November 16, 2016, a Central Animal Facility (CAF) technician discovered that thirteen mice were dead and four mice were in moribund condition in four cages of mice held in the USU CAF. The moribund animals were euthanized immediately by LAM personnel. These mice were part of a study on blood clotting mechanisms, and all had a genetic defect in a protein implicated in the clotting process. A lab member had taken a blood sample from the tail veins of each mouse on the afternoon of Tue 15 November. When the animals were found on 16 November there was blood in the cage, suggesting that the mice might have died from blood loss.
The IACUC chair and IACUC members were given a preliminary briefing on the incident at its scheduled meeting on the same day (16 November). The Chair appointed a subcommittee to investigate the incident. They were charged with investigating the incident, including meeting with the PI and all persons involved in the incident, and developing recommendations for actions to reduce the probability of similar incidents occurring in the future. The subcommittee will report back to the IACUC at its December meeting. A final report on the incident will be submitted to OLAW as soon as the investigation is complete.

Contact person making report:
Brian M. Cox, Ph.D.
Chair, IACUC, USU
(brian.cox@usuhs.edu; telephone #
Institution: Uniformed Services University
(OLAW Assured Facility #A-3448-01)