DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:
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August 30, 2017

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

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 July 28, 2017 letter regarding noncompliance with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals at The Uniformed Services University of Health Sciences. This letter was preceded by a preliminary report to OLAW via email on May 18, 2017. According to the information supplied, OLAW understands that on April 29, 2017, a principal investigator (PI) self-reported a protocol deviation that consisted of administration of two agents not listed on the approved protocol and administration of an approved agent at a different time than what was specified in the protocol. This work involved rats and was reported to be PHS supported.

Corrective actions have been completed which involved the submission and approval of amendments to accurately describe agents and timing of administration in the protocol; PI, co-investigator, and technician re-training using the CITI training course related to protocol compliance; and a meeting with the PI and all the PI's laboratory staff to discuss the importance that all protocols are written with procedures as they are actually performed.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to prevent recurrence of these incidents. We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,

Jane Na, DVM
Veterinary Medical Officer
Office of Laboratory Animal Welfare

cc: IACUC Contact

28 July 2017

Axel Wolff M.S., D.V.M.
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 A3448-01)

Dear Dr. Wolff,

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 18 May 2017.

On the morning of 29 April 2017, a USU Principal Investigator (PI) reported an apparent deviation from protocol on a research project funded by the National Institutes of Health. The USU IACUC conducted the primary initial review of this protocol and the protocol also received secondary review by the United States Army Medical Research Institute of Chemical Defense (USAMRICD) IACUC since part of the work was conducted at USAMRICD. The USAMRICD IACUC Chair discovered the apparent deviation from protocol while reviewing a meeting abstract and raised the issue with the PI.

Since primary approval occurred at USU, the USU IACUC Chair appointed a sub-committee to investigate the incident. The subcommittee noted that part of the protocol involved experiments designed to study the effectiveness of two new anti-epileptic agents for reduction of long-term pathology induced by the nerve agent soman. In the original approved protocol, it is stated that 20 min would elapse after the rats were exposed to soman before administering atropine sulfate (used to minimize peripheral toxic effects). Instead, atropine sulfate was administered 1 min after exposure to soman. In addition to the test drugs covered by the approved protocol, two other drugs were also given to the animals, specifically bispyridinium oxime and caramiphen (an anticholinergic compound). These agents are used to increase survival following seizures and thus permit the analysis of long-term brain pathology induced by soman and the evaluation of protective effects of the test drugs. Neither oxime nor caramiphen treatments were included in the approved protocol.

Because the earlier administration of atropine and the use of the oxime and caramiphen are actually standard practice after exposure to a nerve agent, the subcommittee concluded that the protocol deviation was due to errors in writing the protocol. No

animals were harmed by this deviation and in fact, the protocol as implemented reduced the risk of suffering and death in the animals. The PI immediately met with the USAMRICD IACUC after the deviation was discovered, reported the incident to the USU IACUC Chair, and submitted two minor modifications to the USU IACUC requesting approval of the early administration of atropine and the use of bispyridinium oxime and caramiphen. Both minor modifications have been approved.

After reviewing the original protocol, email correspondence between the USAMRICD IACUC and the USU IACUC Chair and the Director of USU Laboratory Animal Medicine (LAM), the minor modification requests submitted by the PI in response to this incident, and a memorandum from the IACUC documenting approval of the modifications, the subcommittee concluded that the deviation from protocol resulted from an oversight during the writing of the protocol. To reduce the probability of future protocol deviations, the subcommittee recommended:

1) that the PI, and all co-investigators and technicians based at USU who are listed on the protocol, re-take part of the CITI training course relating to protocol compliance;
2) that the PI should also hold a meeting with all persons listed on all her currently active protocols during which they will review all protocols to be sure they accurately reflect the way procedures are actually conducted;
3) that the PI should report back in writing to the USU IACUC after this meeting indicating when the meeting was held by date and time, and including a list of participants, a general overview of the discussion, and documentation of re-training through the CITI training site.

The report of the subcommittee was discussed by the full IACUC at its scheduled meeting on 17 May 2017. After discussion, the Committee voted unanimously to accept the recommendations of the subcommittee. The PI and all investigators in the PIs laboratory at USU have now completed the required retraining. The PI has held a meeting with all laboratory staff to emphasize the importance of ensuring that all procedures be conducted as described in the approved protocol and any amendments, and has submitted a memorandum to the IACUC reporting the meeting. The IACUC now considers this incident closed.

Sincerely,

Secondary individual on behalf of

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

A3448-W

Morse, Brent (NIH/OD) [E]

From: Morse, Brent (NIH/OD) [E]
Sent: Thursday, May 18, 2017 1:45 PM
To: [redacted] OLAW Division of Compliance Oversight (NIH/OD); iacuc@usuhs.edu
Cc: USARMY Ft Detrick MEDCOM USAMRMC Other ACURO [redacted]
Subject: RE: Initial Report of Incident Re Animal Welfare - Uniformed Services University (OLAW Assured Facility #A-3448-01)

Thank you [redacted] We will open a 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: [redacted] mailto:megan.ralls@usuhs.edu]
Sent: Thursday, May 18, 2017 12:52 PM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; iacuc@usuhs.edu
Cc: USARMY Ft Detrick MEDCOM USAMRMC Other ACURO <usarmy.detrick.medcom-usamrmc.other.acuro@mail.mil>; [redacted]@usuhs.edu> [redacted]@usuhs.edu>
Subject: Initial Report of Incident Re Animal Welfare - Uniformed Services University (OLAW Assured Facility #A-3448-01)

Dr. Morse,
I am writing to report a recent incident involving a deviation from protocol in the animal care program at Uniformed Services University, Bethesda MD.
During implementation of a research protocol, investigators administered two drugs not listed in the protocol to rats, and also administered a third drug at a different time during the procedure from the time noted in the approved protocol. Both the unapproved drug treatments and the earlier administration of the third drug had the effect of reducing symptom severity in the test animals during tests with a toxic agent, and were originally planned as part of the experimental design.

Once the PI became aware of the deviation from approved protocol, she brought the issue to the attention of the IACUC. The IACUC Chair has appointed a subcommittee to review the incident and make recommendations to the full IACUC.

A final report will be sent as soon as the investigation has been completed. Let me know if you have any questions or concerns.

Contact Person making report:

Secondary individual
IACUC Administrator
@usuhs.edu
telephone #
Institution: Uniformed Services University
OLAW Assured Facility Number #A-3448-01

Thank you,

Secondary individual
IACUC Administrator
Office of Research Compliance
Uniformed Services University of the Health Sciences
4301 Jones Bridge Road
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