DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

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Office of Laboratory Animal Welfare
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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

March 21, 2022

Re: Animal Welfare Assurance
#A3127-01 (OLAW Case 1G)

Mr. Adam Cohen
Senior Vice President & General Counsel
Oklahoma Medical Research Foundation
825 Northeast 13th Street
Oklahoma City, OK 73104

Dear Mr. Cohen,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 16, 2022 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Oklahoma Medical Research Foundation, following up on an initial telephone report on February 2, 2022. According to the information provided, OLAW understands that one mouse died and others were not doing well after receiving antibiotic water, which had not been described in the approved protocol.

The immediate action taken upon discovery consisted of removing the antibiotic water, counseling the laboratory staff to only conduct procedures as described in the approved protocol, checking the other protocols for noncompliance and confirming that there was none, and requiring the post-doctoral fellow responsible to undertake retraining. The Institutional Animal Care and Use Committee (IACUC) required the two laboratory members involved to take retraining and for all laboratory staff to be counseled to follow the protocol. The laboratory was placed on enhanced post-approval monitoring and the grant was not charged for any unauthorized animal activities.

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 IACUC 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

KEVIN L. MOORE, M.D.
CHAIRMAN
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE

OKLAHOMA MEDICAL RESEARCH FOUNDATION
825 NORTHEAST 13TH STREET
OKLAHOMA CITY, OK 73104-5046
TELEPHONE: 405-271-4347
EMAIL: KEVIN-MOORE@OMRF.ORG

March 16, 2022

Brent Morse, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

Dear Dr. Morse:

The purpose of this letter is to provide you a report regarding a reportable event at the Oklahoma Medical Research Foundation.

The incident was discovered on February 8, 2022. It involved *ad libitum* oral administration of an antibiotic cocktail in water to mice that was not approved by the IACUC and which may have contributed to the death of one mouse. The PI on this study is a full-time faculty member at the Oklahoma Medical Research Foundation. This work was funded by the Public Health Service.

This incident was first reported to Dr. Axel Wolff by telephone on February 22, 2022, by Dr. Kevin Moore, IACUC Chair at the Oklahoma Medical Research Foundation.

A full report of the incident, actions taken and recommended actions of the OMRF IACUC follows.

The Animal Welfare Assurance Number for the OMRF is D16-00080 (A3127-01).

Respectfully,

(b) (6)

Adam Cohen
Institutional Official
Senior VP & General Counsel
Oklahoma Medical Research Foundation

(b) (6)

Kevin L. Moore M.D.
Chairman, Institutional Animal Care and Use Committee
Oklahoma Medical Research Foundation

INCIDENT TIMELINE

Tuesday, February 1, 2022

Comparative Medicine (CM) staff observed that all the mice in two adjacent cages with 5 mice per cage were "mild poor doers". Both cages were marked with "antibiotic water" cards indicating a start date of 1/26/22 and end date of 2/16/22. This was reported by email to research staff as well as veterinary and supervisory staff. The cages were flagged for daily monitoring. The water bottles were activated daily and moistened food provided as per normal facility procedures for mice experiencing mild piloerection or hunched posture. The mice in both cages were on the same AUP supported by PHS funding and were so called "Townes model mice". This strain carries several human hemoglobin knock-in genes replacing the endogenous mouse genes and is used as a model for sickle cell disease.

Wednesday, February 2, 2022

In reviewing the health reports, the AV asked the supervisor how long the mice had been on the antibiotic water and if the cages had purple procedure cards. This question was asked by the AV knowing that this lab does whole body irradiation prior to stem cell transplant and are provided antibiotic water in the peri-transplant period and therefore the cages should have purple procedure cards indicating that the mice had received whole body irradiation. The AV suspected that the mice might be experiencing some transient effects from radiation and/or adapting to the change in water.

Thursday, February 3, 2022

Oklahoma City received 6-8 inches of snow and experienced major road closures. Mice were monitored by on-site animal care staff. No worsening of condition reported.

Friday, February 4, 2022

Supervisor responded that purple procedure cards were not present and reported that all the mice look about the same clinically and they are still very mild poor doers.

Saturday-Sunday, February 5-6, 2022

Mice were monitored by animal care staff. No worsening of condition reported.

Monday, February 7, 2022

One mouse was reported dead in the afternoon while the remaining mice "looked fine".

Tuesday, February 8, 2022

AV examined the remaining mice in the two cages. One had mild piloerection, while the others were clinically normal. Necropsy of the dead mouse revealed extensive cannibalism and autolysis.

Based on the following observations, the AV determined that a protocol violation had likely occurred.

1. The only "antibiotic water" approved on the relevant AUP is associated with whole body irradiation.
2. The signup log for the irradiator indicates that the lab did not use the irradiator in this timeline.

3. The only "antibiotic water" approved on the AUP in question is a pink colored. However, water bags on these two cages in question was colorless.
4. The lab does have a different and colorless "antibiotic water" cocktail approved for use for gastrointestinal studies on a different AUP. However, Townes mice are not used in the studies on that AUP.

The AV contacted the relevant PI and research staff about the situation. They were informed to discontinue "antibiotic water" immediately and that this incident of non-compliance would be reported to the IACUC for further investigation.

PI research staff confirmed that the cages were placed back on standard drinking water within an hour of this notification.

Wednesday, February 9, 2022

The PI distributed a letter to all lab members involved in animal use, reminding them that all lab members are required to follow IACUC policy and to be familiar with the contents of AUPs, etc.

Monday, February 14, 2022

The IACUC Chair requested that the PI complete an internal audit of current animal census to determine if additional issues exist or not and report back to as soon as is reasonably practicable.

Tuesday, February 15, 2022

The PI's senior research staff reported that the audit was completed and did not identify additional compliance issues.

IACUC INVESTIGATION

Two members of the PIs research staff that were involved the use of the mice in question were interviewed separately on Friday, February 18. One is a post-doctoral fellow who was working separately on gastrointestinal studies on a different AUP wanted to do a "pilot experiment" on the hypothesis that the antibiotic cocktail approved on the latter AUP might be clinically beneficial to the Townes mice. The second staff member is a graduate student that maintains the labs breeding colony of Townes mice whose participation was limited to providing the two cages of mice to the post-doc.

The two admitted to the facts as presented above and took responsibility for the fact that their actions were not approved on the relevant AUP.

The training records of the two research staff members were reviewed. Both research staff members had completed all AALAS training modules currently required by OMRF, including the module entitled "*Working with the IACUC*". In addition, both completed the animal facility orientation that OMRF required prior to obtaining access to the facilities.

The post-doctoral fellow entered his position in September 2021 and missed the 2021-22 "Responsible Conduct of Research" training cycle at the OMRF that was given in August 2021 and is scheduled for that training in the fall of 2022.

The graduate student has completed BMSC 5001: *Integrity in Scientific Research* in 2018 training as required by the University of Oklahoma Graduate College and is scheduled to take BMSC 6011: *Integrity in Scientific Research II* in the fall of 2022.

March 15, 2022

The incident was reported to the full committee and discussed. The IACUC agreed with the actions of the Attending Veterinarian and the IACUC Chair to date. However, the IACUC decided that the following additional actions should be taken;

1. The two research staff members involved should repeat all available IACUC-related training modules available on the AALAS Learning Library as soon as practicable.
2. The post-doctoral fellow should enroll and complete the RCR course BMSC 5001: *Integrity in Scientific Research* at the next course availability in the fall of 2022.
3. All the PI's research staff will be required to attend a group meeting to discuss IACUC-related issues with the IACUC Chair and AV.
4. The CM staff will maintain heightened post-approval monitoring of the PI's animal research activities for 6 months. The AV will report to the IACUC monthly and at the end of the 6 months and make a recommendation on ending or continuing heightened post-approval monitoring. The AV will report to the IACUC immediately if any issue arises during this 6-month period.
5. The animal care charges for the two cages are to be charged to an internal funding source.

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, March 18, 2022 7:25 AM
To: Kevin Moore, MD
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: OMRF Incident Report - A3127-01

Thank you for this report, Dr. Moore. We will send a response soon.
Axel Wolff

From: Kevin Moore, MD <Kevin-Moore@omrf.org>
Sent: Thursday, March 17, 2022 2:02 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6) Adam Cohen <Adam-Cohen@omrf.org>; (b) (6) (b) (6)
Subject: [EXTERNAL] OMRF Incident Report - A3127-01

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and are confident the content is safe.

Dr. Morse;

Please find attached a final report of an incident of non-compliance at OMRF. This incident was first reported to Dr. Axel Wolff by telephone on February 22, 2022. Feel free to contact me if you have any questions or concerns. Please confirm receipt to this email.

Best regards,

Kevin L. Moore, M.D.
IACUC Chairman
Oklahoma Medical Research Foundation
(b) (6)
kevin-moore@omrf.org

AG127-16

Office of Laboratory Animal Welfare

OLAW

Initial Report of Noncompliance

By: (b) (6)

Date: 2/22/22

Time: 9:20

Name of Person reporting: Kevin Moore
Telephone #: (b) (6)
Fax #:
Email:

Name of Institution: Oklahoma Medical Research Foundation
Assurance number: A-3127

Did incident involve PHS funded activity? Yes
Funding component: _____
Was funding component contacted (if necessary): _____

What happened?

Procedures conducted on sickle cell mice not approved on protocol, 1 mouse died, others recovering after getting treated water.

Species involved: mice
Personnel involved: Post Doc
Dates and times:
Animal deaths:

Projected plan and schedule for correction/prevention (if known): _____

Retraining PI, counsel, enhanced PAM

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY
Case #_____