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

April 10, 2019

Re: Animal Welfare Assurance
#A3237-01 (OLAW Case 2T)

Ms. Steffani Webb
Vice Chancellor for Administration
Institutional Official
University of Kansas Medical Center
3901 Rainbow Road, MS 2015
Kansas City, KS 66160

Dear Ms. Webb,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 26, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Kansas Medical Center. According to the information provided, OLAW understands that a significant change had been implemented in a rat kidney disease protocol without prior approval by the Institutional Animal Care and Use Committee (IACUC). Specifically, an experimental diet was fed to the rats which resulted in greater mortality than expected.

The corrective actions consisted of temporarily stopping the animal activities and amending the protocol to clarify the procedures, expected clinical signs, and monitoring parameters. The Principal Investigator submitted an adverse event report to the IACUC and was counseled on adhering to the procedures approved in the protocol. The institutional animal user training stresses the requirement for conducting only IACUC approved procedures. This information is also provided to investigators through departmental meetings, post-approval monitoring reviews, and newsletters.

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

A3237-2T

KU MEDICAL CENTER
The University of Kansas

March 26, 2019

Axel Wolff, MS, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive – MSC 7982
Bethesda, MD 20892-7982

Regarding:	**University of Kansas Medical Center -- Assurance #A3237-01**
Research Projects:	**The Mineralization of the matrix in disease and health** **IACUC Number: 2017-2422**
Funding Agency:	**NIH-NIDDK R01-DK11693**

Dear Dr. Wolff:

In accordance with PHS Policy IV.F.3, the University of Kansas Medical Center (KUMC) Institutional Animal Care and Use Committee (IACUC) is reporting an incident of protocol drift and an adverse event.

On 11/27/18, Regulatory Affairs for Biological Sciences (RABS) staff noted a high number (12/38 rats or ~32%) of rat death communications from Laboratory Animal Resources (LAR) to the PI on the Animal Care and Use Proposal (ACUP, aka "protocol") listed above. Upon further investigation by our Post-Approval Monitor (PAM) we learned that a group of 5/6 nephrectomized (Nx) rats had been purchased and enrolled in a study modeling Nephrogenic Systemic Fibrosis (NSF), which was induced by injections of different gadolinium-bound contrast agents (GBCA). Some of these rats were further challenged by being placed upon a high-phosphate diet, which was a change to the experiment that had not been previously reviewed and approved by our IACUC. Although expected clinical signs were described in the ACUP, this additional factor resulted in a rapid and unpredicted increase in the rate of progression of NSF and premature death of these rats.

Study Specific Corrective Action:

The PI temporarily ceased rat NSF studies and presented an adverse event report to the IACUC on 12/19/18. Additionally, in coordination with RABS and LAR veterinary staff, the PI

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developed an addendum to more accurately describe future experiments including the sequence of events, expected clinical signs and monitoring parameters. During the addendum development, several meetings occurred with the Post Approval Monitor and Director of Regulatory Affairs to cover monitoring of protocol drift and ways to prevent reoccurrence. The addendum was submitted on 1/19/19 and approved on 2/19/19.

IACUC and RABS Action:

The adverse event was presented to the convened IACUC on 1/15/19. However, the committee requested additional information as well as the submitted addendum prior to making any determinations. The revised adverse event was discussed at the subsequent monthly IACUC meeting on 2/19/19. In addition, the addendum was presented to the full committee for consideration. The committee voted unanimously to approve the addendum and further determined that the resolution of the adverse event was appropriate. The IACUC determined that the issues identified rose to the level of reportable to OLAW based on the OLAW Guidance notice NOT-OD-05-034. This information is also being provided to the Association for the Accreditation of Laboratory Animal Care (AAALAC).

The IACUC and RABS office will continue to stress the importance of maintaining a compliant research program through IACUC approved activities related to animal use and that all procedures need approval prior to initiation. The issue of protocol drift and working with only approved procedures is a main focus of our Animal User Training. Additional avenues of training include research department meetings, Post-Approval Monitoring reviews and/or additional communications through quarterly newsletters. If you have questions or need more information, please feel free to contact me at (b) (6)

Sincerely,

(b) (6)

Steffani Webb
Vice Chancellor for Administration

cc: (b) (6)
Nathan Culley, DVM, DACLAM, Chair, IACUC
Douglas Brandt, DVM, Executive Director, Laboratory Animal Resources, Attending Veterinarian

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, March 29, 2019 12:39 PM
To: Nathan Culley
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Incident Reports for the University of Kansas Medical Center A3237-01

Thank you for these reports, Dr. Culley. We will send responses soon.
Axel Wolff

From: Nathan Culley <nculley@kumc.edu>
Sent: Friday, March 29, 2019 10:44 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6)
Subject: Incident Reports for the University of Kansas Medical Center A3237-01

Dr. Wolff,

Please find attached, two (2) animal welfare compliance report letters from the University of Kansas Medical Center (A3237-01). Please let me know if you have any further questions regarding the reports.
Have a wonderful weekend.

Regards,

Nathan C Culley, DVM, DACLAM
IACUC Chair
Executive Director, Regulatory Affairs for Biological Sciences
University of Kansas Medical Center
nculley@kumc.edu
(b) (6)