



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive - MSC 7982
Bethesda, Maryland 20892-7982
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

March 26, 2018

Re: Animal Welfare Assurance
#A3348-01 (OLAW Case 1U)

Thomas F. Murray, Ph.D.
Interim Provost
Creighton University
2500 California Plaza
Omaha, NE 68178

Dear Dr. Murray,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 12, 2018 letter reporting the suspension of an animal activity at Creighton University, following up on an initial telephone report on February 22, 2018. According to the information provided, OLAW understands that the Institutional Animal Care and Use Committee (IACUC) took this action after determining that on a cardiovascular surgery study using microswine there was an unacceptably high mortality rate, inadequate oversight by the Principal Investigator, incomplete records, multiple protocol violations, and an inability to obtain sufficient data.

The corrective actions consisted of the IACUC requesting an outside subject matter expert to observe the surgery and make suggestions for improvement which must be incorporated into the protocol. The surgical team must then successfully complete four out of six surgeries to show proficiency and decrease mortality. The Research Compliance Auditor will monitor surgeries, the procedures will be video and audio recorded, the investigators must undertake retraining, the research staff must certify understanding of the protocol, and detailed medical/surgical records will be created and maintained during surgery and subsequently reviewed by the IACUC, Attending Veterinarian, and Research Compliance. Upon successful completion of the corrective actions, the protocol will be reinstated. The NIH funding component was notified about the suspension.

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 on Humane Care and Use of Laboratory Animals.

Sincerely,

(b) (6)

Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare

cc: IACUC Chair

(b) (6)

Robert Gibbens, D.V.M., USDA-APHIS-AC

Creighton UNIVERSITY

Office of the Provost
Research Compliance

March 12, 2018

Dr. Brent Morse
Office of Laboratory Animal Welfare
National Institutes of Health
Division of Compliance Oversight
6705 Rockledge Drive
RKL1, Suite 1050, MSC 7982
Bethesda, Maryland 20892-7982

Re: Creighton's Institutional Animal Care and Use Committee (IACUC) Animal Incident Report,
Assurance Number **A3348-01/D16-00226**

Dear Dr. Morse:

Creighton University is submitting a finalized report regarding a protocol suspension that was the result of a unanimous vote at a convened IACUC meeting on February 19, 2018. The University's Research Compliance Auditor made the initial report to Dr. Wolff via phone on February 22, 2018.

Background Information/Animal Welfare Issue:

Multiple issues were discovered during an investigation that was initiated in response to a request to modify an approved IACUC protocol that utilizes microswine, a USDA-covered species. At the conclusion of the investigation, the IACUC met to discuss five serious non-compliant items that were uncovered; namely, multiple protocol violations, incomplete medical and surgical records, a lack of oversight from the Principal Investigator, an unacceptably high mortality rate, and the inability to obtain sufficient data to make scientifically valid comparisons. After a thorough discussion concerning the severity and number of non-compliant items, the IACUC voted unanimously to suspend the protocol until the following corrective action plan can be successfully completed.

Corrective Action Plan Taken:

At a re-convened meeting on February 26, 2018 the IACUC created and unanimously voted to implement the following corrective action plan. The PI must complete all of the items listed below before the IACUC will consider reinstatement of the experimental protocol:

- The IACUC requests that an expert in microswine cardiovascular surgery visit Creighton University to observe the surgical team perform two survival surgeries on microswine. Any suggestions or advice given by the expert must be incorporated into the experimental protocol for future procedures.
- Following the visit from the cardiovascular expert, the surgical team must successfully complete 4 out of a possible 6 survival off-pump coronary artery bypass graft (CABG) surgeries with full

occlusion of the left anterior descending coronary artery (LAD) in order to demonstrate proficiency and achieve an acceptable mortality rate.

- All survival surgeries that involve harvest of the superficial epigastric vein (SEV) and performing the coronary artery bypass graft procedure will be monitored by the Research Compliance Auditor until further notice from the IACUC.
- In addition to monitoring, all surgical procedures must be video and audio-taped by the surgical team for documentation purposes.
- All personnel must complete re-training of specific CITI modules, in addition to medical/surgical records training.
- A detailed medical/surgical record specific to the coronary artery bypass graft procedure will be created by the surgical team. A non-sterile person will be responsible for taking complete notes during the surgery to document key time points and/or any complications in real time. The PI must review and sign all records immediately after each surgery, and all records will be audited by the attending veterinarian (AV), IACUC Chair, and Research Compliance.
- Following completion of any modifications that are made to the experimental protocol, all personnel will sign a form indicating that they have "read and understood" the protocol in its entirety, and that they also understand that any future protocol deviations or violations will result in permanent protocol suspension.

Reporting:

The following agencies/organizations will be contacted regarding this noncompliance:

- This research is funded under NIH Grant #R01HL128063. Creighton University will follow the NIH guidelines for reporting.
- Since this protocol includes microswine, a USDA-covered species, the United States Department of Agriculture (USDA) will be notified of this noncompliance.
- Additionally, the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) will be informed of this noncompliance.

Please feel free to contact Dr. Thomas F. Murray, Provost and Institutional Official, at (b) (6) or Dr. Joseph A. Knezetic, Director of Research Compliance, at (b) (6) if you have any further questions.

Sincerely,

(b) (6)

Thomas F. Murray Ph.D.
Institutional Official and
Provost

(b) (6)

Joséph A. Knezetic, Ph.D.
Director of Research Compliance

CC: IACUC Chair
Animal Resource Facility Director
Research Compliance Office

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, March 19, 2018 7:35 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Creighton University Protocol Suspension- Assurance # A3348-01

Follow Up Flag: Follow up
Flag Status: Completed

Thank you (b) (6)

Dr. Wolff will respond soon.

Regards,
Joan

From: (b) (6)@creighton.edu]
Sent: Friday, March 16, 2018 2:51 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Murray, Thomas F <tfmurray@creighton.edu>; Knezetic, Joseph A <joek@creighton.edu>; (b) (6)
(b) (6)@creighton.edu>
Subject: Creighton University Protocol Suspension- Assurance # A3348-01

Hello,

Attached please find the written report as follow-up to the initial report made via phone on February 22, 2018 regarding a protocol suspension.

Best Regards,

(b) (6)





Initial Report of Noncompliance

By: an

Date: 2/22/18

Time: 12:30

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

Name of Institution: Craigton U
Assurance number: A3348

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

What happened? Incomplete records, not following protocol, high mortality rate, 60%
Can't collect significant data, lack of oversight

Species involved: SWINE
Personnel involved:
Dates and times:
Animal deaths:

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

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY
Case # _____