



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

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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) 480-3387

May 1, 2020

Re: Animal Welfare Assurance
A3416-01 [OLAW Case 2I]

Pramod Khargonekar, Ph.D.
Vice Chancellor for Research
University of California-Irvine
(b) (4) Aldrich Hall
Irvine, CA 92697-3175

Dear Dr. Khargonekar,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your April 30, 2020 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of California Irvine (UCI). This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the UCI Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to: failure to adhere to IACUC approved protocol. The final report states the experimental design was to evaluate the regenerative ability of the kidney by causing experimental renal damage and subsequent observation of regeneration in pig kidneys. The protocol did not describe use of a ureteral access sheath, but the surgeon used one during the procedure to facilitate access through the ureters. The report states a post-operative stent, which would normally be employed after use of an access sheath, was not employed. On December 16, 2019, the laboratory was performing the one-week post-injury collection on a pig when the surgeon encountered difficulty accessing the ureters with a catheter to collect urine. During the next weekly meeting with the Principal Investigator (PI), the surgeon discussed the access issue and it was revealed that the placement of a ureteral access sheath used to perform the initial renal injury was not approved in the protocol. The PI halted the study and instructed the surgeon to no longer participate in any animal work in the laboratory while he investigated the situation. The PI then informed the IACUC Chair with a summary of his findings on January 15, 2020.

The report states the unapproved procedure was performed on 9 pigs. The PI determined the data collected from these animals was compromised by the use of a ureteral access sheath, which would have caused damage to the ureters. The incident was discussed at the February 13, 2020 convened meeting by IACUC members. The committee considered the PI's request for replacement animals to redo the study. The IACUC required the surgical procedure to be modified and for pre-surgical bloodwork to be added as part of pre-operative care to improve animal monitoring. The request for replacement animals was determined to be scientifically justified. The committee limited the number of animals to two animals as part of a pilot study of the newly modified surgical procedure. It is stated that additional animals after the pilot study may only be requested after submission of a progress report of the pilot study results. Also, protocol modifications related to this noncompliance will be reviewed by the full committee at a future convened meeting.

The committee also determined that a lack of enough oversight within the lab contributed to this incident and required for the PI and a campus veterinarian to be present during the first surgery of the pilot study. A summary of these corrective actions was provided to the PI on March 6, 2020 and he reaffirmed his commitment to comply and will complete the action items required.

It is noted that this study was not supported by PHS funds. Based on its assessment of this explanation, OLAW understands that the University of California, Irvine has implemented appropriate measures to correct and prevent recurrences of these problems and is now compliant with provisions of the PHS Policy. We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,

(b) (6)

Jacquelyn T. Tubbs, DVM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact



Office of Research
141 Innovation, Suite 250
Irvine, CA 92697-7600

April 30, 2020

Brent Morse, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, MD 28092

RE: University of California, Irvine – Animal Welfare Assurance number D16-00259 (A3416-01)

Dear Dr. Morse,

The University of California, Irvine (UCI) is reporting an incident of non-compliance involving protocol deviation of surgical procedures in pigs on an approved animal use protocol (AUP-18-141). No federal funding was used in the conduction of this study.

The experimental design was to evaluate the regenerative ability of the kidney by causing experimental renal damage and subsequent observation of regeneration in pig kidneys. To access the kidneys to cause the damage, the protocol called for a flexible ureteroscope to be inserted up through the urethra into the bladder, then advanced into each ureter and into each kidney. The protocol did not mention use of a ureteral access sheath; however, the surgeon performing the procedure used one to facilitate access through the ureters. A post-operative stent, which would normally be employed after use of an access sheath, was not employed. Following protocol guidelines pigs were re-anesthetized one week after the initial procedure for urine collection directly from each ureter in order to assess the regeneration capacity of the kidney. This procedure was repeated after 6 weeks, at which time the pigs were euthanized.

On December 16, 2019, the laboratory was performing the one-week post-injury collection on a pig when the surgeon encountered difficulty accessing the ureters with a catheter to collect urine. During the next weekly meeting with the Principal Investigator (PI), the surgeon discussed the access issue and it came to light at this time that the placement of a ureteral access sheath used to perform the initial renal injury was not approved in the protocol. The PI halted the study and instructed the surgeon to no longer participate in any animal work in the laboratory while he investigated the situation. The PI then informed the IACUC Chair with a summary of his findings on 1/15/20.

The unapproved procedure (placement of a ureteral access sheath) was performed in a total of 9 pigs. The PI determined that the data collected from these 9 pigs was compromised by the use of a ureteral access sheath, which would have caused damage to the ureters.

IACUC members discussed the incident at the convened meeting held on February 13, 2020, at which time they reviewed details of the animal procedures and experimental timeline and considered the PI's request for replacement animals to redo the study.

To resolve this noncompliance, the committee required the surgical procedure to be modified and for pre-surgical bloodwork to be added as part of pre-operative care to improve animal monitoring. The request for replacement animals was determined to be scientifically justified. Nevertheless, the committee limited

B. Morse, 4/30/20

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the number to two animals, to be part of a pilot study of the newly modified surgical procedure; additional animals after the pilot study may only be requested after submission of a progress report of the pilot study results. Protocol modifications related to this noncompliance will be reviewed by the full committee at a future convened meeting. The committee also determined that a lack of sufficient oversight within the lab contributed to this incident and required for the PI himself and a campus veterinarian to be present during the first surgery of the pilot study.

A summary of these requirements was provided to the PI on 3/6/20, and he reaffirmed his commitment to comply and will complete the resolution action items.

Please feel free to contact me or the IACUC Chair, Dr. Nancy Burley, if you have questions.

Sincerely,

DocuSigned by:
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Pramod Khargonekar, Ph.D.
Vice Chancellor for Research

cc: IACUC Chair N. Burley
Attending Veterinarian C. Lindsell
(b) (6)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, May 1, 2020 7:22 AM
To: IACUC
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Compliance Report -- University of California Irvine D16-00259

Thank you for this report, (b) (6) We will send a response soon.

Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: IACUC <iacuc@uci.edu>
Sent: Thursday, April 30, 2020 7:20 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Pramod Khargonekar <pramod.khargonekar@uci.edu>; Nancy Burley (UCI) <ntburley@uci.edu>; Claire Lindsell <claire.lindsell@uci.edu>; (b) (6)
Subject: Compliance Report -- University of California Irvine D16-00259

Please see attached compliance self-report.

A preliminary report was not submitted to OLAW with regard to this incident. All details, including correction plan, are included in the attached letter.

Sincerely, on behalf of the IACUC,

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UCIrvine

Office of
Research

Institutional Animal
Care & Use Committee

