



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) 402-7065

January 6, 2020

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

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 December 18, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of California, Irvine. According to the information provided, OLAW understands that in May 2019 and again in July 2019 moribund mice were observed on an ocular infection protocol in which viral encephalitis is a relatively common occurrence. Although the protocol contained strict monitoring guidelines during the acute phase of the infection, it was determined that increased monitoring was not taking place. In both instances moribund mice were euthanized immediately. It was determined that the unexpectedly high mortality may have been associated with either very pure virus or a change in the procedures for titration. Also, a mouse strain was used that was not listed on the protocol. It was stated this animal activity was PHS-funded.

It is understood that the corrective action plan included requiring all lab members to review the approved protocol(s) before each experiment and that two lab members will be assigned to each experiment to ensure that someone will be available to monitor the animals. Monitoring will be recorded on a whiteboard in the lab and in an online calendar. If needed, extra monitoring visits will be added. The protocol will be modified to include pilot experiments to assess the different viral strains and dosages. In addition, remedial training must be completed for all members of the research team and training records will be completed and maintained for each member of the lab. The lab will conduct monthly staff meetings for a period of six months.

OLAW appreciates the prompt consideration of this matter by the University of California, Irvine, which was consistent with the philosophy of institutional self-regulation. Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate and correct the deficiency, and to prevent recurrence. **Please be advised** that it is your institution's responsibility to report this incident to the Chief Grants Management Officer of the funding component if it was determined that expenses related to these noncompliant activities were charged to the grant. We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

(b) (6)

Brent C. Morse, DVM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact



A3416-2E
Office of Research
141 Innovation, Suite 250
Irvine, CA 92697-7600

December 18, 2019

Brent Morse, D.V.M.
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, MD 20892

RE: University of California, Irvine - Animal Welfare Assurance # D16-00259

Dear Dr. Morse:

The University of California, Irvine (UCI) is reporting an animal welfare issue involving failure to monitor animals post-procedurally as necessary to ensure their well-being. Funding for the project is provided by NIH grant number 5R01EY026103

The protocol in question (AUP-19-111) involves the ocular infection of mice with herpes simplex virus (HSV). As viral encephalitis is a relatively common occurrence, the IACUC-approved protocol contains strict monitoring guidelines intended to enforce reasonable humane endpoints and avoid unnecessary pain and distress.

The lab experienced unusually high mortality in May 2019; a significant number of mice were noted during a routine facility inspection that were considered moribund. Campus veterinary staff present during the inspection euthanized the mice and counselled the lab staff regarding the need for prompt euthanasia; the principal investigator indicated that they had seen higher-than-normal mortality and were trying to determine the cause. Then in July 2019, campus veterinarians were alerted to another group of dead or moribund animals; review of electronic room-access logs indicated a possible breakdown in the lab's monitoring of these animals. Again, all sick animals were humanely euthanized immediately by veterinary staff.

Considered individually, these incidents may not reach the level of reportable non-compliance; however, the IACUC determined that the multiple instances could reflect a problematic trend in the laboratory, or at least a breakdown in either training or communication. The UCI IACUC discussed these incidents at its convened meeting on August 8, 2019 and appointed a subcommittee to meet with the lab to discuss the matter. During the meeting, the laboratory staff acknowledged the following:

- The unexpectedly high mortality may have been associated with either very pure virus or a change in your procedures for titration.
- A miscommunication between laboratory members resulted in the use of a mouse strain that was not listed in the approved protocol.
- A member of the laboratory staff failed to check on the animals over a 36-hour period during the acute infection period, in spite of the twice per day monitoring schedule listed in the approved protocol.

The Principal Investigator and his staff presented a number of changes to their processes in response to this situation:

- All lab members will review the approved protocol(s) before each experiment.
- Two lab members will be assigned to each experiment to ensure that someone will always be available to monitor the animals at least twice per day during the acute phase of the infection.
- Details of each experiment will be posted on a whiteboard in the lab. Twice-daily monitoring will be recorded both on the whiteboard and in an online calendar.
- If the condition of the animals warrant it, additional monitoring visits will be added (e.g. every 8 hours) during the acute phase of the infection (7-14 days post infection).
- A modification to the protocol will be submitted, adding pilot experiments to assess the different viral strains proposed for use and ensure that the dosages used are appropriate.

The IACUC and the Institution determined the following additional actions were necessary to correct and prevent recurrence of this event:

- The lab will conduct monthly staff meetings and submit a record of attendance and brief summary of topics discussed to the IACUC for a period of six months from the date of this letter.
- The lab will complete and maintain training records for each member of the lab team, in order to provide/maintain documentation of appropriate training.
- All members of the research team must complete remedial training.

Please contact me or the IACUC Chair if you have any questions or concerns regarding this matter.

Sincerely,

DocuSigned by:

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Pramod Khargonekar, Ph.D.
Vice Chancellor for Research

cc: Institutional Animal Care and Use Committee Chair Burley
Attending Veterinarian and Director Lindsell
Associate Vice Chancellor for Research (b) (6)
IACUC Administrator (b) (6)

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, December 19, 2019 2:26 PM
To: 'IACUC'
Subject: RE: University of California Irvine D16-00259

Thank you for providing this final report (b) (6) We will send an official response soon.

Best regards, Brent Morse

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

Please note that this message and any of its attachments are intended for the named recipient(s) only and may contain confidential, protected or privileged information that should not be distributed to unauthorized individuals. If you have received this message in error, please contact the sender.

From: IACUC [mailto:iacuc@uci.edu]
Sent: Thursday, December 19, 2019 12:16 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: University of California Irvine D16-00259

Please see attached compliance self-report.



Office of Research
Winter Administrative Recess - Dec 24, 2019 - Jan 1, 2020