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

December 10, 2019

Re: Animal Welfare Assurance
A3865-01 [OLAW Case W]

Professor Joseph Incandella
Vice Chancellor for Research
University of California-Santa Barbara
Office of Research
(b) (4) Cheadle Hall
Santa Barbara, CA 93106-2050

Dear Dr. Incandela,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your November 25, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of California – Santa Barbara. Your letter supplements the information contained in the preliminary phone report to our office on October 28, 2019. According to the information provided, OLAW understands that on September 8, 2019 a dead mouse was found trapped between a cage lid and the front edge of the feeder. It was determined that the mouse was trapped on September 6th after being returned to the cage by the PI. Another mouse had been found dead in the same cage under similar circumstances on August 29, 2019. In both cases the animals had not completely recovered from the alcohol treatment and had not been monitored according to protocol. It is understood that the animal activity was funded by the PHS.

Corrective and preventive measures included the IACUC determining that an email should be sent to the PI emphasizing the importance of the development of a plan to prevent future noncompliant incidents. In addition, the issue will be addressed as part of a seminar to be presented to the campus animal use community.

OLAW believes that the corrective and preventative measures put in place by the University of California – Santa Barbara are consistent with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals. We appreciate being informed of this unfortunate incident 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

UC **SANTA BARBARA**

Institutional Animal Care and Use Committee

Santa Barbara CA 93106-5062
Tel: (805) 893-5855
Fax: (805) 893-2005
Email: iacuc@lifesci.ucsb.edu
https://www.research.ucsb.edu/compliance/animal-subjects/

November 25, 2019 Animal Welfare Assurance A3865-01 (D16-00497)

Dr. Axel V. Wolff, Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, MD 20892-7982

Dear Dr. Wolff,

In accordance with our Assurance and PHS Policy IV.F.3, I am writing to report an incident of protocol non-compliance involving the care and use of animals at the University of California, Santa Barbara. Below is the full investigation report into protocol #12-18-862.2 regarding the incident preliminarily reported to OLAW via a phone call from our IACUC Chair on October 28, 2019. The IACUC is convinced that appropriate remediations were enacted to prevent recurrence of the incidents described below.

Summary of Investigation:

On September 9, 2019, the IACUC Office was copied on an email from the Animal Resource Center (ARC) Manager to a Principal Investigator (PI) informing him/her that one of her/his mice had been found dead in its cage. The dead mouse was

found trapped between the lid of the cage and the front edge of the feeder on the morning of Sunday, September 8, 2019, by the animal care technician working the weekend. The Attending Veterinarian (AV) conducted a necropsy on the mouse the following day and concluded that it had died due to crushing trauma to the internal organs. The email from the ARC Manager also mentioned that this cage of animals was the same cage where another mouse had been found dead on August 29, 2019, by the ARC staff. That animal was found squeezed between the back of the feeder and the back of the cage. Upon being notified of these incidents, the IACUC Chair appointed a sub-Committee, comprised of himself and the AV, to further investigate these incidents.

On October 2, 2019, the IACUC Chair, Coordinator, and AV met with the PI. The PI explained that this cohort of mice were receiving injections of ethanol and then used for a place-conditioning assay, and that s/he was the only person working with these mice at this time. The PI stated that the mice were still inebriated, but responsive, when placed into their cage and returned to the housing room. When the PI responded to the ARC Manager's September 9th email, s/he described his/her technique for placing mice back into the cage. S/he stated that "the cage lid is slid back only 2-3 inches, just enough to allow a mouse to be placed inside (this avoids its cage-mates escaping)". However, sliding the cage lid back as described would create a gap between the lid and the feeder large enough for a mouse to fit through.

Following the second incident (i.e., on September 8, 2019) of a mouse being found dead in this cage, the PI met with the ARC Manager and showed them his/her technique for placing the lid back onto the cage. The ARC Manager noted that the feeder was not completely seated into the grooves on the top edge of the cage. The ARC Manager explained that if the feeder is not properly seated into the cage, it may create a gap between the feeder and the back of the cage where a mouse could potentially fit and get stuck. This is the area of the cage where the mouse that was found dead on August 29th was discovered. Additionally, if the feeder is not properly seated into the grooves on the top edge of the cage, or if an object (such as a mouse) becomes trapped between the lip of the feeder and the lid, then the

lid will be ajar. This in turn would cause difficulty (i.e., a tight fit) when sliding the cage back into the rack. The PI stated that s/he did not notice any resistance when sliding the cage into the IVC rack on the afternoon of Friday September 6th, which is the last time s/he accessed that cage of mice.

With respect to the dead mouse found on August 29, 2019, the mice were being treated intraperitoneally with ethanol, sometimes with relatively high doses. Mice were responsive, but under the effects of the alcohol when returned to their cages. The description of the assay in the PI's SOP states that "sedation studies will be conducted only when trained laboratory personnel are available to continuously monitor the animals for at least 5 hrs or until the animals are fully recovered". Based on the discussion and a consideration of the design of the cage, the sub-Committee concluded that the most likely scenario to account for the death of this mouse is that the feeder was not properly installed (thereby creating a gap between the feeder and the back of the cage) and that a mouse under the influence of alcohol got itself lodged between the feeder and the back wall of the cage and was unable to get itself out.

With respect to the dead mouse found on September 8, 2019, the sub-Committee considered the possibility that this cage had been accessed by someone other than the PI between the afternoon of Friday (September 6th) and the morning of Sunday (September 8th) when the mouse carcass was found by the animal technician. Upon reviewing the security report of all personnel who accessed that room during that relevant time frame, it was determined that the only other personnel that entered the room after the PI left on Friday September 6, 2019 was the animal care technician working the weekend and a postdoc from another lab whose animals are on a separate IVC rack in the same room. The postdoc stated that s/he did not access the animals in the affected cage on September 6th or subsequently. Additionally, on October 9, 2019, the IACUC Chair, Coordinator, and an IACUC member met with the animal care technician who was responsible for conducting the daily health checks during the weekend of September 7th and 8th. S/he stated that s/he did not open any cages housing mice associated with the PI's lab over the weekend. Additionally, while the technician did identify the animal carcass on

Sunday morning, it was noted that s/he did not identify it during the daily health check on Saturday morning. S/he stated that it is possible that s/he did see the mouse carcass on Saturday while conducting the daily check, but may have thought it was eating while hanging from the feeder or just hanging onto the underside of the lid. The IACUC Chair emphasized the importance of being thorough while checking the health status of each animal.

The ARC has previously not experienced any similar situations in our program that have resulted in animal deaths.

Although the sub-Committee could not unequivocally determine the course of events leading to the death of the mouse discovered on September 8, 2019, the most likely cause of the death would appear to be a mouse jumping up on the food hopper just prior to the lid of the cage being put into place on Friday September 6, 2019 and the animal being crushed between the lid and the front edge of the feeder when the cage was slid back into its place on the rack.

During the October 18, 2019 IACUC meeting, the Chair presented this report to the Committee. The Committee agreed that part of the reason this incident occurred was likely due to the mice not being completely recovered (i.e., sobered) from their alcohol treatment, as described in the approved behavioral assay SOP, prior to being placed back in their cage after the assay. The Committee recommends that the protocol personnel performing this behavioral assay be reminded that all animals must be continuously monitored until they have completely recovered from their drug treatment and prior to being placed back in their home cage and returned to their caging rack. Additionally, the Committee agreed with the sub-Committee that the most likely cause of death was crushing when the lid was last placed back on the cage and it was returned to its rack. Due to other recent noncompliant incidents involving this PI, the Committee voted that a follow-up email should be sent to the PI to emphasize the importance of her/him developing a plan to prevent future noncompliant incidents. The Committee also discussed how incidents such as these will be addressed at an upcoming "continuing education/refresher" seminar to be presented to the campus animal use community

by the Chair to (i) remind everyone of the general principles involved in animal care and use, and (ii) review some of the most common issues that have arisen over the past few years on campus, with the goal of reducing the probability of future incidents. This protocol is funded by NIH grant 1R01AA024044. The Committee voted that this incident is reportable to both OLAW and AAALAC. On October 28, 2019, the IACUC Chair made a preliminary report of this incident via phone call to OLAW's Division of Compliance Oversight.

If you have any additional questions or comments, please feel free to contact us. Thank you for your time.

Sincerely,

(b) (6)

Prof. Joseph Incandela
Institutional Official
Vice Chancellor for Research
(b) (4) Cheadle Hall
University of California, Santa Barbara
Santa Barbara, CA 93106-2050
incandela@research.ucsb.edu

Cc: Dr. Stuart Feinstein, IACUC Chair
Dr. Manuel Garcia, Campus Veterinarian
IACUC Office

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, December 06, 2019 7:29 AM
To: IACUC Office; OLAW Division of Compliance Oversight (NIH/OD)
Cc: Manny Garcia; Stu Feinstein; (b) (6) Joseph Incandela
Subject: RE: Incident Report for A3865-01

Thank you for providing this report. 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

-----Original Message-----
From: IACUC Office [mailto:iacuc@lifesci.ucsb.edu]
Sent: Thursday, December 05, 2019 6:57 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Manny Garcia <manuel.garcia@ucsb.edu>; Stu Feinstein <feinstei@ucsb.edu>; (b) (6) (b) (6); Joseph Incandela <incandela@research.ucsb.edu>
Subject: Incident Report for A3865-01

To Whom It May Concern:

Attached is a letter that details an incident of protocol noncompliance at the University of California, Santa Barbara (A3865-01).
The UCSB IACUC has investigated and reviewed the incident. This report includes the summary of the incident, as well as any Committee corrective actions.

Please let me know if there are any questions.

Sincerely,
(b) (6)

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(b) (6)

A3865-W

Office of Laboratory Animal Welfare

OLAW

Initial Report of Noncompliance

By: [redacted]

Date: 10/28/19 Time: 2:10

Name of Person reporting: George Feinstein, chair

Telephone #: [redacted] (b) (6)

Fax #:

Email:

Name of Institution: U. C. Santa Barbara

Assurance number: A3865

Did incident involve PHS funded activity? _____

Funding component: _____

Was funding component contacted (if necessary): _____

What happened? Dead mouse in cage. Crush injury between cage lid & food hopper. PI accessed cage on Friday before. PI may have crushed mouse by "sliding" cage lid.

Species involved: Mouse

Personnel involved: PI

Dates and times: 9/8/19

Animal deaths: Yes, 1-2 mice

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

Counseling & retraining of PI

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY

Case #_____