Subject: Protocol [redacted] Investigation Report
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 10/9/2018, 12:00 PM
To: [redacted]
CC: Manny Garcia <manuel.garcia@ucsb.edu>, Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, Joseph Incandela <incandela@research.ucsb.edu>

October 9, 2018

To: [redacted]

Cc: Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela

From: [redacted], IACUC [redacted], on behalf of the IACUC

Re: Final Report of Protocol [redacted] Investigation

Attached is the IACUC's final updated report based on the sub-Committee's findings for the recent investigation into the protocol [redacted] rat euthanasia incident. The IACUC voted that the incident was not reportable to oversight agencies (i.e., OLAW, AAALAC) and that the corrections were appropriate.

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

--
[redacted], UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_report_final.pdf 82.2 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On April 25, 2018, four laboratory rats were prematurely euthanized on teaching protocol [redacted]. On May 10 2018, the protocol PI/course instructor notified the IACUC, and the IACUC Chair formed a sub-Committee to investigate this unforeseen outcome.

On June 5, 2018, the sub-Committee met with the PI, the head TA, and the TA that euthanized the rats. On April 24, 2018, the head TA sent instructions via email to the other TA, indicating which rats should be euthanized for the students' surgical training. The other TA stated that, due to extenuating personal circumstances, s/he did not read the entire email before s/he inadvertently euthanized the wrong cohort of rats on the following day, April 25, 2018. The PI stated that the undergraduate students enrolled in the course were still able to able to complete all aspects of the lab, despite having fewer rats with which to work. This was accomplished by using one less rat per experimental condition, which was workable, but not ideal.

The sub-Committee determined that this incident was a result of human error. The PI has since instructed his/her TAs to be more mindful of the procedures they are conducting and to seek out assistance when necessary. The Chair summarized and presented this report to the IACUC at the September 14, 2018 meeting, and the IACUC determined that the steps the PI took to reduce the probability of a similar incident occurring again were appropriate. The IACUC also determined that this incident does not meet the conditions for requiring a report to be sent to OLAW or AAALAC.

PROTOCOL (PI being investigated)

Principal Investigator: [redacted]	Phone: X [redacted]
Co-PI:	Phone:
Complete IACUC #: [redacted]	IACUC Title: [redacted]
Species/Strain: Sprague Dawley Rats	Current housing location: ARC [redacted] Vivarium

EVALUATION BY IACUC

☐ No further investigation warranted – Date:_____

☒ Proceed with investigation

☒ Notify Institutional Official

☒ Sub-Committee Appointed: 1. IACUC Chair

2. Attending Veterinarian

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: September 14, 2018

☒ Final IACUC action – Date: September 14, 2018

☒ Notifications required (list): IO, PI, AV, IACUC Chair

☒ Notifications sent - Date: October 9, 2018

Subject: Protocol [redacted] Investigation Report
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 10/9/2018, 12:03 PM
To: [redacted]
CC: Manny Garcia <manuel.garcia@ucsb.edu>, Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, Joseph Incandela <incandela@research.ucsb.edu>

October 9, 2018

To: [redacted]

Cc: Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela

From: [redacted], IACUC [redacted], on behalf of the IACUC

Re: Final Report of Protocol [redacted] Investigation

Attached is the IACUC's final updated report based on the sub-Committee's findings for the recent investigation into the protocol [redacted] incident of non-compliance. The IACUC voted that the incident was not reportable to oversight agencies (i.e., OLAW, AAALAC) and that the corrections were appropriate.

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

--
[redacted] UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_report_final.pdf 85.2 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On June 5, 2018, a Principal Investigator (PI) submitted a modification to the IACUC Office and Attending Veterinarian (AV) for review. During the pre-review process, the AV reviewed the number of mice produced by the PI's breeding colony and determined that s/he had exceeded the number of mice approved for use by the IACUC. On July 2, 2018, the PI sent an email to the IACUC Chair, estimating that the number of mice bred on the protocol was about 500-600. At the time, the protocol was approved for the use of 350 mice.

On July 5, 2018, a sub-Committee appointed by the IACUC Chair met with the PI in question. The PI explained that s/he had underestimated the number of mouse lines that were needed for the experiment, as well as underestimating the number of mice needed to keep the lines going. During the meeting, the PI explained that while s/he assigned a lab technician to manage the breeding program, the technician had not been instructed to track the number of animals being produced. It should be noted that the PI is a relatively new faculty member here at UCSB (an Assistant Professor) with little experience managing an animal breeding colony. The PI mentioned that animal breeding colony procedures at his/her previous laboratory at a different institution were quite different than here at UCSB, and that now that s/he had a better understanding of the UCSB procedures, s/he would endeavor to avoid any further similar issues in the future.

Since becoming aware that the number of mice bred have exceeded the amount approved by the IACUC, the PI has appointed a member of her/his lab to be in charge of tracking the animal census. During the meeting with the sub-Committee, the PI mentioned that s/he will soon submit a protocol modification to request and justify an increase in the number of animals required for the conduct of his/her research program. On July 6, 2018, the IACUC Office received a modification request from the PI to increase the animal numbers.

The sub-Committee recommends that the ARC [redacted] review their orientation procedures to emphasize the details of colony management for appropriate new personnel.

During the September 14, 2018 IACUC meeting, the IACUC Chair summarized and presented this report to the Committee. The IACUC agreed that the sub-Committee's recommendations to the ARC [redacted] to minimize the probability that a similar situation would occur again were appropriate. Prior to the IACUC meeting, the IACUC Coordinator was able to confirm that, during the time the animal census exceeded their approved numbers, the PI's NIH grants had not been used to pay the ARC for housing his/her mice. Therefore, this incident was determined to be not reportable to OLAW.

PROTOCOL (PI being investigated)

Principal Investigator:	Phone:
[redacted]	X[redacted]

Co-PI: N/A	Phone: N/A
Complete IACUC #: [redacted]	IACUC Title: [redacted]
Species/Strain: Mice	Current housing location: [redacted] Room

EVALUATION BY IACUC

- ☐ No further investigation warranted – Date:_____
- ☒ Proceed with investigation
- ☒ Notify Institutional Official
- ☒ Sub-Committee Appointed: 1. Stu Feinstein
  2. Manuel Garcia
- ☒ Report of Investigation (by Sub-Committee to the IACUC) submitted
- ☒ Convened IACUC meeting review - Date: September 14, 2018
- ☒ Final IACUC action – Date: September 14, 2018
- ☒ Notifications required (list): PI, AV, IO, IACUC Chair
- ☒ Notifications sent - Date: October 9, 2018

Subject: Protocol [redacted] Investigation Report
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 11/16/2018, 4:11 PM
To: [redacted]
CC: Manny Garcia <manuel.garcia@ucsb.edu>, Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, Joseph Incandela <incandela@research.ucsb.edu>

November 16, 2018

To: [redacted]

Cc: Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela

From: [redacted], IACUC [redacted], on behalf of the IACUC

Re: Final Report of Protocol [redacted] Investigation

Attached is the IACUC's final updated report based on the sub-Committee's findings for the recent investigation into the protocol [redacted] incident of a vole found deceased in a trap. The IACUC voted that the incident was not reportable to oversight agencies (i.e., OLAW, AAALAC) and that the actions taken by the PI were appropriate.

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

--
[redacted] UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_report2_final.pdf 100 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation

On March 11, 2018, the IACUC Office received an email from a PI, informing the IACUC that a wild vole had been found dead by a TA in a Sherman trap on March 7, 2018. The PI instructs an [redacted] undergraduate course with one of the course objectives being to teach students how to trap and handle small vertebrate animals for mark/recapture abundance surveys. For one week during the course, the TAs and students go to [redacted], located near UCSB, in the mornings and check traps that had been set the previous evening by a TA. Upon being notified of the incident, the IACUC Chair formed a sub-Committee to investigate the details.

On April 11, 2018, the sub-Committee met with the PI, the head TA and the TA that was responsible for setting and checking the traps on the date in question. On March 6, 2018, the TA set the traps just before 6 PM (i.e., within the hour before sunset). When the same TA checked the traps with students at around 8 AM the following morning, s/he found that 9 animals had been trapped, including the one vole that was found dead. None of the other trapped animals were dead, including a second vole. The PI and TAs confirmed that the traps had been set and checked according to the procedures described in the protocol. The TA brought the carcass back to their lab and stored it in the freezer in case the Attending Veterinarian (AV) chose to perform a necropsy.

During the meeting, the TA noted that the vole was relatively small, compared to other voles, and this could have contributed to its mortality. The PI also confirmed that s/he checked the weather forecast that week and the low temperature for the day was predicted to be 50°F; however, when the PI checked the recorded temperature for the evening of March 6th, the low was measured at 45°F. While colder than expected, the PI stated that s/he did not expect 45°F weather to cause a mortality. One potential improvement to the trapping procedure that the sub-Committee discussed with the PI and TAs was the possibility of adding bedding or grass to the bottom of the Sherman trap so that trapped animals can avoid direct contact with the metal floor. However, the PI mentioned that bedding and grass inside of the trap tends to get caught in the hinges and makes it difficult to keep the trap clean.

Additionally, the PI referenced a study published in the *Wildlife Society Bulletin* (*WSB*) showing that voles (i.e., Arvicoline rodents) caught in Sherman traps do experience a higher mortality rate than *Peromyscus* spp, the most common genus of animal captured in the [redacted] course (Stephens, R.B. & Anderson, E.M. Effects of trap type on small mammal richness, diversity, and mortality. *WSB*, 2014, **38**(3):619–627). The sub-Committee agreed with the PI that the most likely cause of death was stress due to trapping.

During the May 18, 2018 IACUC meeting, the IACUC Chair presented this investigation report to the IACUC at a convened meeting and led a discussion about the incident. The IACUC concurred with the sub-Committee and the PI that stress due to trapping was the most likely cause of death and that all of the proper trapping procedures had been followed. The IACUC voted that no corrective actions were warranted and that this incident was not reportable.

PROTOCOL (PI being investigated)

Principal Investigator: [redacted]	Phone: X [redacted]
Co-PI: N/A	Phone: N/A
Complete IACUC #: [redacted]	IACUC Title: [redacted]
Species/Strain: Vole	Current housing location: N/A

EVALUATION BY IACUC

☐ No further investigation warranted – Date:_____

☒ Proceed with investigation

☒ Notify Institutional Official

☒ Sub-Committee Appointed: 1. IACUC Chair

2. Attending Veterinarian

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: May 18, 2018

☒ Final IACUC action – Date: May 18, 2018

☒ Notifications required (list): PI, IO, AV, IACUC Chair, [redacted]

☒ Notifications sent - Date: November 16, 2018

Subject: Protocol [redacted] Investigation Report
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 11/20/2018, 10:16 AM
To: [redacted]
CC: Joseph Incandela <incandela@research.ucsb.edu>, Manny Garcia <manuel.garcia@ucsb.edu>, Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, [redacted]

November 20, 2018

To: [redacted]

Cc: Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela; [redacted]

From: [redacted], IACUC [redacted], on behalf of the IACUC

Re: Final Report of Protocol [redacted] Investigation

Attached is the IACUC's final updated report based on the sub-Committee's findings for the recent investigation into the protocol [redacted] incident of two mice that were found dead in their cage. The IACUC voted that the incident was not reportable to oversight agencies (i.e., OLAW, AAALAC) and that the actions taken by the ARC were appropriate.

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

--
[redacted], UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_report_final.pdf 90.7 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On March 26, 2018, the IACUC Office received an email from the ARC [redacted], informing the IACUC that two mice had been found dead in their cage: a male on Sunday, March 25th, and a female on the morning of Monday, March 26th. The pair of mice had been a breeding pair that had been setup on March 14th. In the email, the ARC [redacted] mentioned that the Hydropac had not been properly punctured and a lack of access to water was likely the reason for the deaths. Upon being notified of the incident, the IACUC Chair formed a sub-Committee to investigate the details.

On April 10, 2018, the sub-Committee met first with the [redacted] in charge of animal care for the room who had worked on Friday, March 25th and then the Attending Veterinarian (AV). The [redacted] stated that s/he changed the cage in question on Friday, March 23rd. While s/he did recall changing the cage, s/he cannot specifically remember toggling the Hydropac valve for that particular cage. However, it should be noted that this is a standard part of procedures in the ARC. The reason the [redacted] did remember that particular cage of mice is because s/he thought they looked relatively small for their age (DOB 1/2/18). The [redacted] stated that s/he recalled ripping the nestlet into smaller pieces and put a couple of food pellets on the floor of the cage for easy access because the mice appeared to be smaller than expected. Next, the sub-Committee met with the AV. The AV stated that he was unable to definitively determine the cause of death because the carcasses had become too decomposed to perform a necropsy.

On April 17, 2018, the sub-Committee met with the ARC [redacted] and the [redacted] that had worked over the March 24-25th weekend. On March 25, the [redacted] found the dead male mouse in the cage as well as its sick littermate. After removing the carcass from the cage, s/he attended to the sick mouse by placing a piece of DietGel on the floor of the cage, removing a small piece of the DietGel to form a basin and filling the basin with water. The female mouse immediately began drinking the water provided. The [redacted] submitted a clinical call report for the remaining sick mouse and sent a text message to the Attending Veterinarian to notify him of the situation. S/he also stated that s/he thought that the mice looked small for their age. The sub-Committee next met with the ARC [redacted]. On March 26th, the ARC [redacted] found the female mouse dead when s/he went to check the sick mouse reported by the technician the previous day. The ARC [redacted] noted that it was possible that the [redacted] back on Friday, May 23rd may have been distracted by ripping up the nestlet and putting food on the floor of the cage causing him/her to forget to toggle the Hydropac valve. The ARC [redacted] also confirmed that the mice had been received in the ARC on March 6, 2018.

The sub-Committee concluded that the most likely cause of death was lack of access to water because the Hydropac had not be properly punctured and that this had not been noticed because the technician had not toggled the nipple. To reduce the probability of a recurrence in the future, the IACUC sub-Committee recommends that the ARC [redacted] re-emphasize to their [redacted] the importance of ensuring that every Hydropac valve is tested by toggling upon introduction into a cage. While it is clearly very unfortunate that the Hydropac was not properly setup in the mouse cage and was the most likely cause of the two deaths, the IACUC also notes that this is the first Hydropac incident caused by [redacted] error in almost three years. During these three years,

well over a hundred thousand Hydropacs have been changed by the [redacted] with little to no animal welfare issues. Additionally, it is notable that during the meeting with the [redacted] in charge of the animal room, s/he showed genuine remorse that the Hydropac did not function properly and resulted in animal deaths.

During the September 14, 2018 IACUC meeting, the IACUC Chair summarized and presented this report to the Committee. The IACUC agreed that incidents such as this, while rare, are essentially inevitable when caring for such a large volume of animals. The IACUC agreed that the ARC [redacted] re-emphasizing the importance of ensuring that every Hydropac is properly set up was appropriate for this incident and did not require further corrective action. The IACUC [redacted] is still trying to determine whether this protocol was funded by the PI's NIH grant at the time of incident. During the October 19, 2018 IACUC meeting, the AV mentioned that the *per diem* rates for these animals are actually paid directly to the ARC by the collaborating institute and not through the Sponsored Projects Office. After consulting with the PI's lab administrator, the UCSB IACUC [redacted] was put in contact with the IACUC [redacted] from the collaborating institute. Following further discussion with the IACUC [redacted] from the collaborating institute, the UCSB IACUC [redacted] was able to determine that while NIH funds were used to pay for the animal *per diem* charges during the incident, the collaborating institute would categorize this as a situation "not normally required to be reported" to OLAW, as per the guidance in NOT-OD-05-034. At the November 16, 2018 IACUC meeting, the IACUC [redacted] detailed his/her discussion with the collaborating institute's IACUC [redacted], explaining that the collaborating institute did not think reporting the incident is necessary. Based on this information, the UCSB IACUC concluded that this incident was not reportable.

PROTOCOL (PI being investigated)

Principal Investigator: [redacted]	Phone: X [redacted]
Co-PI:	Phone:
Complete IACUC #: [redacted]	IACUC Title: [redacted]
Species/Strain: B6/J Mice	Current housing location: [redacted] Vivarium

EVALUATION BY IACUC

☐ No further investigation warranted – Date:_____

☒ Proceed with investigation

☒ Notify Institutional Official

☒ Sub-Committee Appointed: 1. IACUC Chair

2. 007

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: September 14, 2018

☒ Final IACUC action – Date: November 16, 2018

☒ Notifications required (list): AV, PI, IO, IACUC Chair, IACUC [redacted] of collaborating institute

☒ Notifications sent - Date: November 20, 2018

Subject: Final Reports of Frog and Rabbit Incidents
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 2/15/2019, 11:04 AM
To: Manny Garcia <manuel.garcia@ucsb.edu>
CC: Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, Joseph Incandela <incandela@research.ucsb.edu>, [redacted]

February 15, 2019

To: Dr. Manuel Garcia

Cc: Dr. Stuart Feinstein; Dr. Joseph Incandela; [redacted]

From: [redacted], IACUC [redacted], on behalf of the IACUC

Re: Final Reports of Frog and Rabbit Incidents

Attached are two IACUC reports based on recent incidents. One incident being a shipment of frogs that was delivered to the UCSB ARC with multiple deceased and moribund frogs. The other incident being a rabbit that was delivered to the UCSB ARC with a spinal injury. The IACUC reviewed these reports at convened meetings and agreed that these incidents did not require further investigation by a sub-Committee.

Please review the attached reports and if there are any questions, contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

--
[redacted], UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

ARC_frog_investigation_final.pdf	97.1 KB
ARC_rabbit_investigation2_final.pdf	89.3 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On November 7, 2018, the Animal Resource Center (ARC) received a shipment of twenty male and twenty-two female *Xenopus tropicalis* frogs. Upon opening the two crates containing female frogs, an ARC [redacted] discovered that there were multiple dead frog carcasses in the crates. The ARC [redacted] received help from a [redacted] in removing the animals from the crates, separating the healthy female frogs from any deceased or moribund frogs. The ARC [redacted] placed the moribund frogs in warm water in an effort to revitalize them. At that point, the ARC [redacted] was notified, who in turn notified the Attending Veterinarian (AV). After examining the frog carcasses, the AV hypothesized that the frogs had become hypothermic during their shipment to UCSB. The AV then immersed the deceased and moribund frogs in a buffered MS-222 solution to confirm death and provide humane euthanasia, respectively.

On November 7, 2018, the ARC [redacted] sent an email to the IACUC Office reporting the discovery of thirteen frogs that were found either dead or moribund upon their arrival at the ARC. On November 8, 2018, the ARC [redacted] sent a follow-up email reporting that two more of the frogs from this shipment had been found dead that morning. On November 13, 2018, the IACUC Chair and [redacted] met with the AV, ARC [redacted] and [redacted] that had received the frogs. The [redacted] that had assisted with receiving the frogs was away on vacation. The ARC [redacted] mentioned that there were four smaller boxes (two with males and two with females) contained and shipped within a larger box that was lined with newspaper and packing peanuts. During this meeting, the AV mentioned that the frog carcasses were relatively fresh, indicating that they had died not long before being uncrated in the ARC.

The frogs were shipped via [redacted] (i.e., air freight) from a [redacted] animal supply facility in [redacted]. The ARC has been purchasing frog specimens and husbandry supplies from this vendor for multiple years without previous incident. On November 8, 2018, the ARC [redacted] contacted [redacted] to determine if there had been any issues during the shipping process that may have led to the frogs becoming hypothermic. During the call, the [redacted] representative was adamant that hypothermia was not the cause of death for the frogs, but did not have an alternate explanation for the deaths. When ordering the animals, the ARC had requested that the frogs be shipped on Monday, November 5th, so that they would arrive on Tuesday, November 6th. While the shipping label had been printed on November 5th, the representative confirmed that the frogs had been placed in the crate on November 6th. The representative stated that they would send another shipment of frogs to replace the ones that had died during shipment. On November 12, 2018, one of the male frogs that had been received from the original shipment was found dead. It is not apparent whether or not this mortality was related to being shipped the previous week. On November 15, 2018, the ARC [redacted] received an email from the [redacted] stating that the low temperatures (i.e., ≤32°F) in [redacted] were something they should have been watching before shipping the frogs. S/he also stated that they would not be sending replacement animals to the ARC until later in 2019 when the weather was warmer. Based on the facts presented, the IACUC Chair determined that further investigation into the incident was not necessary.

PROTOCOL (PI being investigated)

Principal Investigator:	Phone:
Co-PI:	Phone:
Complete IACUC #:	IACUC Title:
Species/Strain:	Current housing location:

EVALUATION BY IACUC

☒ No further investigation warranted – Date: November 13, 2018

☐ Proceed with investigation

☐ Notify Institutional Official

☐ Sub-Committee Appointed: 1._____

2._____

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: December 14, 2018

☐ Final IACUC action – Date:

☒ Notifications required (list): AV, IACUC Chair, IO, [redacted]

☒ Notifications sent - Date: February 15, 2019

UCSB IACUC INVESTIGATION CHECKLIST

SOURCE (Who is submitting the report?):

Name:	Phone:
Manny Garcia	(805) 893-7344
Department:	Email:
Animal Resource Center (ARC)	Manuel.garcia@ucsb.edu

Summary of Investigation:

On December 4, 2018, the IACUC received an email from the ARC [redacted] reporting an incident involving a New Zealand White rabbit that had been received by two [redacted] that morning. On December 10, 2018, the IACUC Chair and [redacted] met with the [redacted] involved to determine the details of the incident. On December 11, 2018, the Attending Veterinarian emailed his details from the incident to the IACUC Chair. Their accounts of the incident are as follows:

A shipment of twelve rabbits from [redacted] arrived in the ARC. Cardboard crates containing the rabbits were delivered to the rabbit housing room, [redacted] Upon opening one of the crates and removing the rabbits, one of the [redacted] noted that one of the rabbits had soft stool on its side of the shipping crate (each shipping crate contains two rabbits, separated by a cardboard barrier). Once the [redacted] placed the rabbit in its cage, the animal did not pull its hind-legs under itself and dragged its hind-quarters as it moved about the cage. The [redacted] immediately notified the [redacted], who was also in the room, weighing rabbits. The [redacted] immediately called the AV to inform him that an animal required his immediate attention. While waiting for the AV to arrive at the vivarium, the [redacted] administered acepromazine to sedate the animal. Upon examining the animal, the AV determined that it had a spinal fracture, and he euthanized the animal for humane reasons. He was able to confirm the presence of a spinal fracture during the post-mortem examination. While he was not able to determine how long it had been since the rabbit sustained the injury, he was able to determine that it had happened prior to it being received by the ARC.

The [redacted] reported that the euthanized rabbit was at an appropriate weight at the time of receipt and that there were no issues with the other eleven rabbits in the shipment. The [redacted] that removed the rabbit from its shipping crate noted that there was no apparent damage to the crate or the cardboard barrier separating the two rabbits. Additionally, the AV inspected the crate and confirmed that the rabbit had been consuming the diet gel provided for the transit. During a previous incident involving an injured rabbit some time ago, the AV had stated that while rabbit spinal fractures are relatively rare, it is possible for the injury to be self-inflicted. Specifically,, a rabbit can injure its own back if it kicks its hind legs out hard enough and strains its back muscles.

The rabbits are shipped in a temperature-controlled truck from a [redacted] facility in [redacted]. Animals depart from the facility on a Friday and arrive at the UCSB ARC the following Tuesday morning, which makes it, approximately, a four day transit. The animals may be transferred to a second truck during transit. The ARC [redacted] has since contacted the vendor to determine if there were any issues or abnormalities during the transit; the vendor confirmed that there were no issues during the entire trip. While this vendor has been used as the ARC's primary supplier of rabbits,

this is the second time an incident of this nature has occurred within the past two years. In July 2017, a rabbit shipped from the same facility was received by ARC [redacted] with a similar infirmity, paralysis of the hind-quarters. Similarly, the rabbit was quickly euthanized for humane reasons. The AV reported that he has been in communication with the veterinarian for the vendor, who has assured him that they take these reports seriously and strive to prevent these injuries. They stated that they will investigate the matter further on their end and get back to the AV.

At the January 18, 2019 IACUC meeting, the IACUC Chair presented the above report to the rest of the Committee. The IACUC agreed that the injury was most likely self-inflicted during the shipping process and should be considered an accident. The IACUC considers this incident as not reportable to OLAW, USDA, or AAALAC. On January 21, 2019, the AV received an email from the [redacted] in [redacted] regarding the results of their investigation into the incident. After reviewing log books and reports, s/he was unable to discover any specific incidents that may have startled or caused distress in the animals during the shipping process.

PROTOCOL (PI being investigated)

Principal Investigator:	Phone:
Co-PI:	Phone:
Complete IACUC #:	IACUC Title:
Species/Strain:	Current housing location:

EVALUATION BY IACUC

- ☒ No further investigation warranted – Date: December 10, 2018
- ☐ Proceed with investigation
- ☒ Notify Institutional Official
- ☐ Sub-Committee Appointed: 1._____
  2._____
- ☒ Report of Incident (by Sub-Committee to the IACUC) submitted
- ☒ Convened IACUC meeting review - Date: January 18, 2019
- ☐ Final IACUC action – Date:_____
- ☒ Notifications required (list): AV, IACUC Chair, [redacted], IO
- ☒ Notifications sent - Date: February 15, 2019

Subject: Protocol [redacted] Investigation Report
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 2/28/2019, 10:38 AM
To: [redacted]
CC: Manny Garcia <manuel.garcia@ucsb.edu>, Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, Joseph Incandela <incandela@research.ucsb.edu>, [redacted]

February 28, 2019

To: [redacted]

Cc: Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela; [redacted]

From: [redacted], IACUC [redacted], on behalf of the IACUC

Re: Final Report of Protocol [redacted] Investigation

Attached is the IACUC's final report based on the sub-Committee's findings for the recent investigation into the protocol [redacted] incidences of rats running out of medicated water. The IACUC voted that the incident was not reportable to oversight agencies (i.e., OLAW, AAALAC) and that the actions taken by the PI were appropriate.

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

--
[redacted], UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_report_final.pdf 97.4 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On December 13, 2018, the [redacted] received an email from the Animal Resource Center (ARC) [redacted] informing the IACUC Office that there had been multiple instances in which rats on protocol [redacted] had run out of medicated water that is provided to them as part of their experiment. Lab personnel are responsible for providing this medicated water to the rats, not the ARC staff. At the time of the email, four of the five rat cages were out of water. A few days earlier, three of the rat cages were out of water. The ARC [redacted] then forwarded to the IACUC office five other emails (dated July 31, August 17, September 19, September 26, and October 14) that s/he had previously sent to the postdoc in charge of the lab's rat experiments, notifying her/him that their rats were out of medicated water. The PI does not personally work directly with the animals, however s/he was copied on the ARC [redacted] emails to the postdoc. The IACUC [redacted] informed the IACUC Chair of the situation, who stated that he would bring it to the IACUC at their regularly scheduled meeting to be held the following day (December 14, 2018).

According to protocol [redacted], [redacted] Research staff are almost always responsible for providing animals with experimentally required, alternative husbandry (e.g., non-standard diet, water, lighting, etc.) in the ARC, unless specific arrangements have been made by the lab with the ARC staff. However, in the event that the ARC staff finds an empty water bottle in a cage during their routine husbandry responsibilities and they are unable to contact the lab in a timely manner, they replace the water in the bottle with non-medicated water, as occurred in some of these incidents.

At the Friday, December 14, 2018 IACUC meeting, the Chair provided background on this project and summarized the situation for the Committee. The Committee discussed the possibility of suspending the protocol immediately or allowing the study to continue under tightened scrutiny and providing the lab with the opportunity to be heard prior to making a decision on suspension. Additionally, the Chair stated that the IACUC would be performing a formal investigation into the matter after the winter break. Further, to minimize the possibility of additional incidents during the upcoming holiday break, the Chair stated that he would meet with the PI and the postdoc as soon as possible during the following week regarding the overall situation and new post-approval monitoring measures that would be implemented immediately. The Committee voted by a majority not to suspend the protocol, but to put it under greater scrutiny. Multiple IACUC members voted against this course of action and were in favor of suspending the protocol immediately. On December 15, 2018, the Chair sent an email to the PI and postdoc informing them of the above events.

On Tuesday, December 18, 2018, the IACUC Chair, another IACUC member, and the IACUC [redacted] met with the PI and the postdoc. The PI was under the impression that the multiple water availability issues had occurred because of leaking water bottles. However, according to reports from the ARC [redacted] and staff, while there were some incidents of leaking water bottles, most of the cases in which rats were found without medicated water were not caused by leaky

bottles. Rather, the bottles had not been checked and changed in a timely manner. It was on these occasions that the ARC [redacted] would email the postdoc about the empty bottles.

Following extensive discussion, the following post-approval monitoring plan was implemented, effective immediately. First, the IACUC Chair instructed the lab to begin keeping a daily log of all visits to the rats, noting whether or not there was available medicated water for each cage of rats at the time of the visit and also noting whenever a medicated water bottle was changed. This log is to be kept in the room with the animals. Second, to address the possibility of leaking bottles, the IACUC Chair instructed the lab to return to the animal room to check on recently changed water bottles about 30 to 120 minutes after new bottles are placed in a cage to ensure they have not leaked. These additional checks of the water levels should also be documented in the new daily logbook. The lab and ARC staff have also been coordinating their efforts to ensure that any water bottles/caps that are identified as leaky are removed from circulation. Third, the lab also agreed to provide two bottles of water rather than one for each cage, providing a backup in the event of a leak that is not detected. Finally, the lab/postdoc will send a weekly report to the IACUC to report on the absence or presence of water related issues or other issues related to the husbandry of the rats.

The postdoc stated that some of the incidents had been caused by miscommunication between him/her and some of the undergraduate students working in the lab who assisted with the rat husbandry. In order to avoid future miscommunication, the postdoc stated that s/he has begun using Google Docs to maintain a schedule for checking the rats and that this schedule has been shared with all the involved undergrads.

The postdoc mentioned that s/he would be out of town for a couple of days during the winter holiday break. S/he has coordinated with the ARC staff ahead of time to ensure that the rats will continue to receive medicated water during this time.

On January 22, 2019, the Chair, AV, and the IACUC [redacted] met with all personnel involved in the incidents. First, they met with the PI and the postdoc. The postdoc stated that s/he checks the water bottles about half of the time and undergraduates working in the lab check the water bottles the other half of the time. The postdoc re-iterated that at least some of the water issues arose because of scheduling miscommunication among the personnel responsible for checking the rats over the weekends and that implementing Google Docs should remedy this problem. The postdoc confirmed that the lab has now been completely filling (as opposed to partially filling) the bottles with medicated water and has been logging their checks of the rats and when water bottles are refilled. Since the meeting on December 18, 2018, the postdoc stated that all conditions of the post-approval monitoring plan had been implemented. No issues were identified during the past month. This post-approval monitoring will continue until at least the investigation report is reviewed by the IACUC at an upcoming meeting.

The sub-Committee next met with the ARC [redacted] and the animal technicians that have found the rat's water bottles empty. The ARC [redacted] confirmed that these incidents most often occurred on weekends. The IACUC Chair encouraged the ARC [redacted] to come forward to the IACUC sooner with these sorts of issues in the future. When a rat cage is found without water, the ARC [redacted] inform the postdoc via email and provide the rats with non-medicated water. The ARC [redacted] confirmed that s/he and the [redacted]s are able to determine when an empty water bottle had not been refilled when necessary as opposed to when it leaks by checking how damp

the rat's bedding is beneath the water bottle. The bedding is much damper when the water bottle leaks than when the rat has consumed all of the water. One of the [redacted] mentioned that the rats would often seem very thirsty when found with an empty water bottle and would immediately begin drinking once provided with more water. The [redacted] in charge of caring for the rat housing room confirmed that s/he has been checking the daily log kept by the lab to confirm that they have been checking the water levels. The IACUC [redacted] will periodically check the lab's log as well.

The IACUC Chair presented this investigation report to the IACUC at a convened meeting on February 15, 2019. The sub-Committee confirmed that they have been receiving the required weekly reports from the postdoc and that no further incidents have occurred since the post-approval monitoring plan had been implemented. The Committee discussed the possibility of suspending the protocol, but determined it to not be necessary at this time. The Committee also found it to be appropriate to leave the post-approval monitoring procedures in place until the Committee determines otherwise. This will be discussed during future convened meetings, where the IACUC Coordinator will provide updates to the Committee on the post-approval monitoring process.

PROTOCOL (PI being investigated)

Principal Investigator: [redacted]	Phone: (805) 893-[redacted]
Co-PI:	Phone:
Complete IACUC #: [redacted]	IACUC Title: [redacted]
Species/Strain: Rats	Current housing location: [redacted]

EVALUATION BY IACUC

☐ No further investigation warranted – Date:_____

☒ Proceed with investigation

☒ Notify Institutional Official

☒ Sub-Committee Appointed: 1. Stu Feinstein

2. Manny Garcia

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: February 15, 2019

☒ Final IACUC action – Date: February 15, 2019

☒ Notifications required (list): AV, IACUC Chair, PI, IO, [redacted]

☒ Notifications sent - Date: February 28, 2019

Subject: Protocol [redacted] Investigation Report
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 6/4/2019, 3:57 PM
To: [redacted]
CC: [redacted], Manny Garcia <manuel.garcia@ucsb.edu>, Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, Joseph Incandela <incandela@research.ucsb.edu>, [redacted]

June 4, 2019

To: [redacted]

Cc: [redacted]; Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela; [redacted]

From: [redacted], IACUC [redacted], on behalf of the IACUC

Re: Final Report of Protocol [redacted] Investigation

Attached is the IACUC's final updated report based on the sub-Committee's findings for the recent investigation into the incident of animals not being used as described in your approved IACUC protocol [redacted]. The IACUC voted that the incident is reportable to OLAW and AAALAC, and copies of this report will be sent to them.

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

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[redacted], UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_report_final.pdf 90.8 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On April 3, 2019, the IACUC Office received a forwarded message from the PI regarding his/her mice in the vivarium. The [redacted] had emailed the PI to notify her/him that the mice on her/his protocol were now one month past the experimental endpoint identified in their IACUC protocol. While the ARC staff had been hired by the PI to administer an experimental compound to the mice, the experimental treatment schedule was set by the PI and the ARC staff was responsible only for administering the experimental compound at bi-weekly (twice per week) intervals. The experimental compound was prepared and delivered by the lab to the ARC before each treatment (i.e., bi-weekly). The PI notified the IACUC Office that they would be euthanizing all of the mice in their colony within twelve days. The IACUC Chair subsequently asked to meet with the PI to regarding the change in the experimental endpoint for the mice.

The mice being used on the protocol were a transgenic strain, rTg4510, which is a commonly used model for studying the formation of neurofibrillary tangles associated with Alzheimer's disease and related neurodegenerative tauopathies such as frontotemporal dementia. These mice exhibit experimentally useful neurological phenotypes (impaired spatial learning and memory) and a potentially distressful phenotype in later stages (>6.5 months of age) in the form of progressive motor function abnormalities (amyotrophy and motor disturbance). From the protocol: [redacted] The endpoint outlined in the protocol states that an experimental compound (Cinnamaldehyde) will be tested for its ability to "alleviate/attenuate both tau tangles and behavioral pathology" at 6-6.5 months of age, "since this is the time at which memory dysfunction has been reported for this mouse model". The mice were to be euthanized for tissue collection at 6.5 months of age.

The IACUC Chair appointed a sub-Committee, comprised of himself and the Attending Veterinarian (AV), to investigate this potential incident of protocol non-compliance. On April 15, 2019, the IACUC [redacted], Chair and AV met with the PI and another faculty member who had been enlisted to perform the euthanasia and tissue collection procedures. The PI confirmed at the meeting that all of the mice in this experiment (approximately 80 animals) had been euthanized. When asked why these mice were not euthanized according to the experimental endpoint described in the protocol, the PI stated that s/he was not aware of the birthdates of the mice (i.e., s/he had not been tracking their ages). The PI explained that the mice needed to undergo behavioral testing prior to the tissue collection, however, the faculty member who was to perform the behavioral testing procedures for the PI had not started the testing early enough to complete it prior to the experimental endpoint. The PI confirmed that s/he was not planning on using any more animals under this protocol, unless requested by journal article reviewers.

After meeting with the PI, the [redacted], Chair and AV met with the [redacted]. S/he confirmed that the ARC had been administering the experimental compound to the mice according to the treatment plan set by the PI. While the [redacted] and the AV confirmed that no mice had been exhibiting symptoms of the potentially distressful phenotype, the [redacted] did mention that the mice were not looking as bright and active as they had been in previous months.

During the April 19, 2019 convened IACUC meeting, the IACUC Chair summarized the situation for the Committee and led a discussion of whether or not this incident was reportable to OLAW. This project is funded by an NIH grant ([redacted]). Following a discussion, the Committee voted that this incident should be reported to OLAW according to the Guidance of Prompt Reporting outlined in OLAW NOT-OD-05-034. A preliminary report via phone call was made to OLAW's Division of Compliance Oversight by the IACUC Chair on May 3, 2019.

During the May 17, 2019 convened IACUC meeting, the IACUC Chair summarized the discussion with OLAW's Division of Compliance Oversight, noting that they had specifically asked about remediation to prevent similar incidents in the future. The IACUC will require a signed statement from the PI and all personnel listed on the training roster attesting that they have read the protocol and will read all subsequent modifications. If the PI submits another IACUC protocol application in the future, s/he and all personnel on that protocol will be required to sign a similar attestation. The IACUC Chair also stated that he is planning on creating an assurance statement, based on the protocol assurance statement that PI's are already required to sign, that must be signed by all researchers working with animals to affirm that each of them has read and understands the procedures in the protocol and all applicable modifications. The final version of this investigation report will be sent to OLAW and AAALAC.

PROTOCOL (PI being investigated)

Principal Investigator: [redacted]	Phone: X [redacted]
Co-PI: [redacted]	Phone: X [redacted]
Complete IACUC #: [redacted]	IACUC Title: [redacted]
Species/Strain: Tg4510 Mice	Current housing location:

EVALUATION BY IACUC

☐ No further investigation warranted – Date:_____

☒ Proceed with investigation

☒ Notify Institutional Official

☒ Sub-Committee Appointed: 1. Stu Feinstein

2. Manny Garcia

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: May 17, 2019

☒ Final IACUC action – Date: May 17, 2019

☒ Notifications required (list): IO, PI, Co-PI, AV, IACUC Chair, [redacted], OLAW, AAALAC

☒ Notifications sent - Date: June 4, 2019

Subject: Protocol [redacted] Investigation Report
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 6/20/2019, 2:11 PM
To: [redacted]
CC: [redacted] Joseph Incandela <incandela@research.ucsb.edu>, Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, Manny Garcia <manuel.garcia@ucsb.edu>, [redacted], [redacted]

June 20, 2019

To: [redacted]

Cc: [redacted]; Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela; [redacted]

From: [redacted], IACUC [redacted] on behalf of the IACUC

Re: Final Report of Protocol [redacted] Investigation

Attached is the IACUC's final updated report based on the sub-Committee's findings for the recent investigation, for the failure to report a deceased animal to the Attending Veterinarian in a timely manner, of the approved IACUC protocol [redacted].

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

--
[redacted], UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_report_final.pdf 90.9 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On May 4, 2019, the Attending Veterinarian (AV) reported to the IACUC Office the mortality of a swell shark that was being housed at the [redacted] facility. The mortality was reported to the AV via a call from the [redacted]) on or around May 3rd; however, the shark had died the previous week, on April 26th. The [redacted] reported that the cause of death may have been related to a failure of the seawater flow through system caused by a campus-wide computer network outage that occurred on the afternoon of April 24th. The carcass had been discarded prior to notifying the AV of the mortality, so no post-mortem examination was possible. The IACUC Chair appointed a sub-Committee to investigate this incident.

On May 13, 2019, the sub-Committee met with the [redacted] the [redacted], and the [redacted]. On the early afternoon of April 24th, the campus network went offline causing the Metasys system, which monitors and controls the seawater flow through system, to stop functioning. In addition to controlling the seawater flow through the aquarium systems, the Metasys system is supposed to automatically send text and email alarms to the [redacted] when there is a problem with the seawater flow, which did not happen. The reason for the lack of notification needs to be addressed. More importantly, Metasys must notify FM when there is a failure with the system. The seawater flow through system provides filtered, oxygenated seawater to multiple laboratories and aquatic housing facilities on the UCSB campus. Later that afternoon, an intern at the [redacted] reported to the [redacted] that there was no seawater flow and that some of the tank water levels were dropping. The [redacted] contacted Facilities Management (FM) to determine the cause of the flow through system malfunction. The seawater flow was restored approximately 1-1.5 hours after reporting the issue to FM.

The [redacted] stated that the following morning, on April 25th, the shark appeared to be normal. However, that afternoon, an intern notified the [redacted] that a shark was on its back. The male shark was in a tank with two larger female swell sharks, a lobster, and two fish, but none of the other animals were exhibiting health issues. No other animals in other tanks in the facility appeared to be affected by the interruption of seawater flow. The [redacted] informed the [redacted] and [redacted] who later arrived at the [redacted] to examine the shark. The [redacted] noted that while the shark's respiration was normal, it had a yellowish tinge which may have indicated that the water's dissolved oxygen levels were too low. The [redacted] noticed that the flow rate to the tank was low, despite being closer to the seawater supply line than other tanks in the [redacted] that had higher flow rates. The shark was seen earlier in the day swimming near the top of the tank, while the rest of the animals in the tank were resting on the bottom. This is unusual because there should have been a higher level of dissolved oxygen closer to the surface of the water. The [redacted] placed an aerator stone in the tank to increase the dissolved oxygen levels while trying to determine the cause of the low seawater flow rate. The swell shark was then moved to a separate (i.e., quarantine) tank to mitigate the chance of disease transmission to the other animals, should the cause be due to a pathogen. Before leaving that evening, the [redacted] reported to the [redacted] that s/he believed that the shark had died.

The [redacted] stated that on the morning of April 26th, s/he was able to confirm the death of the shark. The [redacted] noted that the AV had previously asked the [redacted] to not freeze animal carcasses on which a necropsy might be performed but that the [redacted] does not have a refrigerator large enough to store a carcass of this size. The [redacted] attempted to keep the carcass fresh for post-mortem examination by the AV by leaving it submerged in cold seawater. However, by the afternoon the carcass had decomposed enough that the [redacted] did not think the AV would be able to use it for his exam, so he placed it in a black trash bag and disposed of it in a dumpster. Further, the [redacted] explained that the AV usually wants to perform a necropsy and send out tissue samples for analysis when there are obvious pathogens involved in the mortality. The [redacted] stated that since the likely cause of death was due to insufficient oxygen supply, s/he thought that the AV would not need to perform a necropsy in this instance.

The IACUC Chair reminded the [redacted] of the importance of promptly reporting both sick and dead animals to the AV. Further, the Chair emphasized that the animal carcass should have been appropriately stored until the AV could perform a necropsy or determined that a post-mortem examination was not needed. The [redacted] noted that the facility does not have a refrigerator large enough to store larger animals. The IACUC suggests that the [redacted] make arrangements with nearby laboratories to use existing cold rooms or similar facilities if similar extenuating circumstances arise in the future. The [redacted] was apologetic about the situation and agreed that these are important matters that will be handled properly in the future (if such situations arise) but did not have a good explanation for the failure to do so in this incident.

It is critical that the seawater system work, and that is has a reliable back up mechanism. The IACUC requests a report from the [redacted] (in a timely manner) describing the state of the back up mechanism. Is it operational so that we are unlikely to have a repeat incident? If not, what efforts are anticipated to make it operational, and with what time line? Is there emergency power for the system? Is there emergency power redundancy?

Finally, the IACUC reminds the Facility personnel that operation of a satellite facility such as the [redacted] requires compliance with all relevant procedures. In the event of future incidents, it is essential that they be reported promptly.

PROTOCOL (PI being investigated)

Principal Investigator: [redacted]	Phone: X [redacted]
Co-PI:	Phone:
Complete IACUC #: [redacted]	IACUC Title: [redacted]
Species/Strain: Swell Shark	Current housing location: [redacted]

EVALUATION BY IACUC

☐ No further investigation warranted – Date:_____

☒ Proceed with investigation

☒ Notify Institutional Official

☒ Sub-Committee Appointed: 1. Stu Feinstein

2. Tod Kippin

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: June 12, 2019

☒ Final IACUC action – Date: June 12, 2019

☒ Notifications required (list): IO, PI, Facility Director, IACUC Chair, AV, [redacted]

☒ Notifications sent - Date: IO, PI, Facility Director, IACUC Chair, AV, [redacted] (June 20, 2019)

Subject: Protocol [redacted] Investigation Report
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 6/20/2019, 2:18 PM
To: [redacted]
CC: Joseph Incandela <incandela@research.ucsb.edu>, Manny Garcia <manuel.garcia@ucsb.edu>, Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, [redacted]

June 20, 2019

To: [redacted]

Cc: Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela; [redacted]

From: [redacted], IACUC [redacted] on behalf of the IACUC

Re: Final Report of Protocol [redacted] Investigation

Attached is the IACUC's final updated report based on the sub-Committee's findings for the recent investigation into the incident of a surgical procedure not being performed by a procedurally proficient or properly supervised surgeon, on your approved IACUC protocol [redacted]. The IACUC voted that the incident is reportable to OLAW and AAALAC, and copies of this report will be sent to them.

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

--
[redacted] UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_report_final.pdf 90.5 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On Sunday April 21, 2019, an [redacted] noted that a rat recovering from surgery (craniotomy and cephalic implant) was lethargic and inactive, placed a pink Sick Card on the animal's cage and submitted a Clinical Call.

On Monday, April 22, 2019, the AV examined the rat and found it to be alert, active, recovering normally from surgery and not exhibiting signs of pain. The AV reviewed the surgery and post-operative recovery record and later contacted the PI and graduate student to ask several questions regarding missing or unclear documentation in these records, including: 1) Was the SpO2 really at 100% at each of the time points?, 2) Was the respiration rate being monitored during surgery?, 3) Was the body temperature being monitored and controlled during surgery?, 4) How much buprenorphine was administered, and when?, 5) How much bupivacaine was administered, and when?, 6) At what times on Sunday was the animal observed?, and 7) At what times on Sunday did the animal receive banamine? The graduate student responded that body temperature was not monitored, but a heating pad was used at all times; both bupivacaine and buprenorphine were administered preoperatively at 2 mg/kg and 0.05 mg/kg, respectively; and banamine was administered to the animal before and after surgery on April 20th, and again on April 21st and 22nd.

On April 25, 2019, the AV, IACUC Chair, PI and graduate student met to review these questions and issues.

On April 29, 2019, the IACUC Chair appointed a sub-Committee, comprised of himself and the AV, to investigate this incident further.

On May 7, 2019, the AV, IACUC Chair, and [redacted] met with the PI and the graduate students and postdoc. One of the graduate students stated that s/he performed the surgery (craniotomy and cephalic implant) on April 20, 2019 without trainer supervision, since s/he believed that s/he was approved to perform this surgery (craniotomy and cephalic implant) without direct supervision because s/he had previously completed a competency evaluation with the AV for a different surgical procedure (jugular vein catheterization and vascular access port implantation). The AV explained that researchers must complete a separate competency evaluation for each surgical procedure to be performed. The graduate student will continue to train on this surgical procedure under the direct supervision of the PI (trainer).

Additionally, the graduate student and PI misunderstood the treatment intervals for the postoperative banamine injections. The protocol states that "banamine or meloxicam and buprenorphine will be injected either before or during the surgical procedure, and then again (meloxicam or banamine) 1-2 times daily for at least 48 hrs after surgery". The graduate student confirmed that all of these analgesic treatments were administered and that s/he provided 4 injections of banamine to the rat within 48 hours of the surgery, but that the banamine treatments were not administered at 12h intervals. The times that these injections were administered is not recorded on the rat's postoperative record. Further, buprenorphine and bupivacaine treatments

were also not documented on the rat's surgery record, nor was the rat's respiration rate monitored during surgery.

In an effort to prevent similar incidents in the future, the sub-Committee recommends that the PI revise his/her surgical training program to better familiarize the researchers conducting surgery on his/her protocols with the many details and expectations presented in the IACUC Guideline on Aseptic Rodent Surgery and Post-operative Care. The AV has notified all PIs performing similar survival surgical procedures on rats, and using banamine as an analgesic, about the availability of an alternative and more practical oral NSAID treatment (Carprofen MediGel). Additionally, the AV and IACUC will review and revise the rodent surgery guideline clarifying surgery training requirements, competency evaluations, and record keeping requirements. Finally, the IACUC wishes to emphasize that any person conducting surgeries for which they are not properly qualified and approved may be removed from the protocol.

This protocol is funded by two NIH grants ([redacted] and [redacted]). The UCSB Sponsored Projects Office (SPO) will work with the PI and NIH to ascertain if any grant money was used during this incident of protocol non-compliance.

PROTOCOL (PI being investigated)

Principal Investigator: [redacted]	Phone: X [redacted]
Co-PI:	Phone:
Complete IACUC #: [redacted]	IACUC Title: [redacted]
Species/Strain: Rat	Current housing location: [redacted]

EVALUATION BY IACUC

☐ No further investigation warranted – Date:_____

☒ Proceed with investigation

☒ Notify Institutional Official

☒ Sub-Committee Appointed: 1. Manny Garcia

2. Stu Feinstein

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: June 12, 2019

☒ Final IACUC action – Date: June 12, 2019

☒ Notifications required (list): IO, PI, AV, IACUC Chair, [redacted], OLAW, AAALAC

☒ Notifications sent - Date: IO, PI, AV, IACUC Chair, [redacted] (June 20, 2019)

Subject: Protocol [redacted] Investigation Report - Updated
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 6/20/2019, 4:10 PM
To: [redacted]
CC: [redacted] Manny Garcia <manuel.garcia@ucsb.edu>, Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, Joseph Incandela <incandela@research.ucsb.edu>, [redacted]

June 20, 2019

To: [redacted]

Cc: [redacted]; Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela; [redacted]

From: [redacted], IACUC [redacted] on behalf of the IACUC

Re: Final Updated Report of Protocol [redacted] Investigation

Attached is the IACUC's final updated report based on the sub-Committee's findings for the recent investigation into the incident of animals not being used as described in your approved IACUC protocol [redacted]. The IACUC voted that the incident is reportable to OLAW and AAALAC, and copies of this report will be sent to them.

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted]

Thank you,
[redacted]

--
[redacted] UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_remediation_final.pdf	56.7 KB
[redacted]_investigation_report_updated_final.pdf	91.4 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On April 3, 2019, the IACUC Office received a forwarded message from the PI regarding his/her mice in the vivarium. The [redacted] had emailed the PI to notify her/him that the mice on her/his protocol were now one month past the experimental endpoint identified in their IACUC protocol. While the ARC staff had been hired by the PI to administer an experimental compound to the mice, the experimental treatment schedule was set by the PI and the ARC staff was responsible only for administering the experimental compound at bi-weekly (twice per week) intervals. The experimental compound was prepared and delivered by the lab to the ARC before each treatment (i.e., bi-weekly). The PI notified the IACUC Office that they would be euthanizing all of the mice in their colony within twelve days. The IACUC Chair subsequently asked to meet with the PI to regarding the change in the experimental endpoint for the mice.

The mice being used on the protocol were a transgenic strain, rTg4510, which is a commonly used model for studying the formation of neurofibrillary tangles associated with Alzheimer's disease and related neurodegenerative tauopathies such as frontotemporal dementia. These mice exhibit experimentally useful neurological phenotypes (impaired spatial learning and memory) and a potentially distressful phenotype in later stages (>6.5 months of age) in the form of progressive motor function abnormalities (amyotrophy and motor disturbance). From the protocol: "pathological lesions (mature tangles) are observed beginning at 2.5 months of age, and memory dysfunction is observed at 4.5 months". The endpoint outlined in the protocol states that an experimental compound (Cinnamaldehyde) will be tested for its ability to "alleviate/attenuate both tau tangles and behavioral pathology" at 6-6.5 months of age, "since this is the time at which memory dysfunction has been reported for this mouse model". The mice were to be euthanized for tissue collection at 6.5 months of age.

The IACUC Chair appointed a sub-Committee, comprised of himself and the Attending Veterinarian (AV), to investigate this potential incident of protocol non-compliance. On April 15, 2019, the IACUC [redacted] Chair and AV met with the PI and another faculty member who had been enlisted to perform the euthanasia and tissue collection procedures. The PI confirmed at the meeting that all of the mice in this experiment (approximately 80 animals) had been euthanized. When asked why these mice were not euthanized according to the experimental endpoint described in the protocol, the PI admitted that it was due to (his own) human error. One of the collaborating investigators was not yet ready to carry out their studies as previously planned, and consequently it was necessary to hold on to the animals longer than expected. Amidst this procedural adjustment, the PI admitted that he inadvertently overlooked the date of euthanization (March 7, 2019) stated in the most recent modification to the animal protocol. The PI confirmed that s/he was not planning on using any more animals under this protocol, unless requested by journal article reviewers.

After meeting with the PI, the [redacted] Chair and AV met with the [redacted]. S/he confirmed that the ARC had been administering the experimental compound to the mice according to the treatment plan set by the PI. While the [redacted] and the AV confirmed that no mice had been exhibiting symptoms of the potentially distressful phenotype, the [redacted] did mention that the mice were not looking as bright and active as they had been in previous months.

During the April 19, 2019 convened IACUC meeting, the IACUC Chair summarized the situation for the Committee and led a discussion of whether or not this incident was reportable to OLAW. This project is funded by an NIH grant ([redacted] Following a discussion, the Committee voted that this incident should be reported to OLAW according to the Guidance of Prompt Reporting outlined in OLAW NOT-OD-05-034. A preliminary report via phone call was made to OLAW's Division of Compliance Oversight by the IACUC Chair on May 3, 2019.

During the May 17, 2019 convened IACUC meeting, the IACUC Chair summarized the discussion with OLAW's Division of Compliance Oversight, noting that they had specifically asked about remediation to prevent similar incidents in the future. The IACUC will require a signed statement from the PI and all personnel listed on the training roster attesting that they have read the protocol and will read all subsequent modifications. If the PI submits another IACUC protocol application in the future, s/he and all personnel on that protocol will be required to sign a similar attestation. The IACUC Chair also stated that he is planning on creating an assurance statement, based on the protocol assurance statement that PI's are already required to sign, that must be signed by all researchers working with animals to affirm that each of them has read and understands the procedures in the protocol and all applicable modifications. The final version of this investigation report will be sent to OLAW and AAALAC.

This protocol is funded by an NIH grant ([redacted]. The UCSB Sponsored Projects Office (SPO) will work with the PI and NIH to ascertain if any grant money was used during this incident of protocol non-compliance.

PROTOCOL (PI being investigated)

Principal Investigator: [redacted]	Phone: X [redacted]
Co-PI: [redacted]	Phone: X [redacted]
Complete IACUC #: [redacted]	IACUC Title: [redacted]
Species/Strain: Tg4510 Mice	Current housing location:

EVALUATION BY IACUC

☐ No further investigation warranted – Date:_____

☒ Proceed with investigation

☒ Notify Institutional Official

☒ Sub-Committee Appointed: 1. [redacted]

2. Manny Garcia

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: May 17, 2019

☒ Final IACUC action – Date: June 12, 2019

☒ Notifications required (list): IO, PI, Co-PI, AV, IACUC Chair, [redacted], OLAW, AAALAC

☒ Notifications sent - Date: June 4, 2019; updated report sent to IO, PI, Co-PI, AV, IACUC Chair, and [redacted] on June 20, 2019

Subject: Protocol [redacted] Investigation Report
From: IACUC Office <iacuc@lifesci.ucsb.edu>
Date: 7/30/2019, 3:03 PM
To: [redacted]
CC: Stu Feinstein <stu.feinstein@lifesci.ucsb.edu>, Manny Garcia <manuel.garcia@ucsb.edu>, Joseph Incandela <incandela@research.ucsb.edu>, [redacted]

July 30, 2019

To: [redacted]

Cc: Dr. Manuel Garcia; Dr. Stuart Feinstein; Dr. Joseph Incandela; [redacted]

From: [redacted], IACUC [redacted], on behalf of the IACUC

Re: Final Report of Protocol [redacted] Investigation

Attached is the IACUC's final report based on the sub-Committee's findings for the recent investigation into the incident of two [redacted] rats that were not euthanized according to the endpoints defined in your approved IACUC protocol #[redacted]. The IACUC voted that the incident is reportable to AAALAC, and a copy of this report will be sent to them.

Please review the attached report and if there are any questions, please contact the IACUC Office at the above e-mail or by phone at 805-893-[redacted].

Thank you,
[redacted]

--
[redacted], UCSB
Santa Barbara, CA 93106-5062
(805)893-[redacted] (office)
(805)893-2005 (FAX)
https://www.research.ucsb.edu/compliance/animal-subjects/

Attachments:

[redacted]_investigation_report_final.pdf 97.8 KB

UCSB IACUC INVESTIGATION CHECKLIST

Summary of Investigation:

On April 5, 2019, an ARC animal care technician reported a clinical abnormality (potential small abscess and scab on chest or elbow) in a [redacted] rat (ID #T501M). That same day, the AV visually examined the animal but was unable to confirm that there was an abscess or skin lesion on this animal. The AV requested that an appointment be arranged with the lab in order to examine the animal under general anesthesia. The rat continued to be monitored by ARC animal care technicians on a daily basis. [redacted] rats are very aggressive wild rats, and are routinely and briefly anesthetized by the lab for experimental manipulations (e.g., blood collection). The research team member responsible for the care and use of this animal colony was notified by email on 4/5/19, 4/11/19, and 4/18/19 regarding the request to anesthetize this animal. The rat was anesthetized by the ARC staff and examined by the AV on 4/18/19. During this examination, several large palpable masses, and an enlarged bladder were identified. The animal was euthanized for humane and diagnostic reasons. A necropsy was performed by the AV revealing several large peritoneal abscesses adhering to and involving the genito-urinary system. Samples were collected for histopathology and bacteriology, the results of which were received on 4/30/19 and 5/2/19 and confirmed that this animal had multiple peritoneal bacterial (Pasteurella sp. and Staph aureus) abscesses.

On April 19, 2019, the IACUC Office was copied on an email exchange between the AV and the lab seeking to determine the cause or contributing factors of the clinical problem in this animal. The lab promptly summarized their experimental RBG (random blood glucose) and body weight data. The AV retrospectively reviewed this data from the lab on the most severely diabetic (RBG >500 mg/dL) animals in the colony and determined that two severely diabetic rats in this colony had suffered from nearly identical clinical problems. The other rat, #522, had been found dead by the ARC animal care staff on March 19, 2019. The necropsy record revealed that this other rat had a couple of large hepatic abscesses (S. aureus was isolated). There was no evidence of an infectious disease of colony health significance in any of the sentinel health monitoring results for this colony.

On May 3, 2019, the IACUC [redacted], Chair and AV met with the lab personnel responsible for the care and use of these animals. The IACUC was seeking to determine why the experimental endpoint and the humane endpoint monitoring plan described in the protocol were not followed for these two diabetic animals. Specifically, the experimental endpoint requires euthanasia one month after reaching an RBG >500 mg/dL on a routine monthly blood collection. The humane endpoint monitoring plan requires increased monitoring frequency (weekly) of RBG levels and body weights following an RBG >500 mg/dL on the routine monthly blood collections. The increased monitoring is continued until there is a 5% drop in body weight or an RBG decrease >100 mg/dL, which is the point when the animal should be euthanized. The lab summarized their experiments with their large [redacted] rat colony, and explained that an Excel spreadsheet with programmed algorithms (macros) was used to identify and track diabetic animals that require increased monitoring. A daily report is printed to show which animals need to be weighed and/or have an RBG test that day. When an animal has a measured RBG level of over 500 mg/dL, the spreadsheet should identify that this animal now requires weekly RBG and body weight

measurements. When a lab member next inputs the animal's weekly RBG and body weight measurements, the spreadsheet should then identify whether there has been a significant enough drop in body weight or RBG level to require the animal to be euthanized. However, the lab stated that there has been an error in the spreadsheet algorithms, and that the two diabetic rats described above were not flagged as needing to be monitored more frequently. Additionally, the lab indicated that they believed that the animals needed to be euthanized only if they reached the cutoff identified in the humane endpoint monitoring plan.

While the lab indicated that they do not know how to fix the spreadsheet algorithms, the colony size and overall number of diabetic animals has shrunk enough for the lab to be able to manually track (i.e., without the use of algorithms) the RBG levels and body weights of animals that require more frequent monitoring. Additionally, the lab indicated that the focus of their diabetes research has shifted, and that they are looking at earlier time points in the disease initiation and progression process. There are currently no severely diabetic animals (RBG >500 mg/dL) remaining in the colony. The endpoints currently defined in the protocol are more specific to identifying and monitoring complications from severe diabetes, such as significant drops in RBG level or body weight associated with ketoacidosis. As the study focus has changed, the Chair has recommended re-evaluating the experimental endpoints and humane monitoring plan.

The AV mentioned that this species is prone to causing self-harm (i.e., over grooming), most likely due to their relatively recent change from being a wild species to a laboratory animal. The AV and ARC staff have tried and continue to try multiple types of enrichment to discourage this behavior, within the restrictions imposed by the scientific requirements of the research (i.e., cellulose-based enrichments have not been allowed), but this has not prevented the problem, and animals that cause serious harm to themselves are euthanized. The skin wounds from self-harm can be difficult to distinguish from diabetic complications (skin ulcers), either of which may have contributed to or caused the internal abscesses that were identified in these diabetic animals, or less likely it may have been a spontaneous illness unrelated to the diabetic phenotype of this animal model. Unfortunately, since this wild rodent is not widely used in biomedical research, there is little to no literature on their husbandry and care, diabetic complications (skin lesions or internal abscesses), stereotypy, or spontaneous diseases.

On May 7, 2019, the IACUC Chair summarized this adverse event investigation and the potential noncompliance (lapses in following the humane endpoint monitoring plan described in the protocol) in an email to the IO and recommended that we self-report this event to our USDA-APHIS VMO (Veterinary Medical Officer).

On May 9, 2019, the IO responded that he agreed with IACUC's self-report recommendation, and further suggested that we should look at finding or developing a more reliable software package for managing large animal populations because a spreadsheet-based program is very prone to these kinds of problems.

On May 10, 2019, the potential noncompliance was reported to USDA-APHIS by the IACUC Chair. The primary question from the USDA VMO following the self-report was whether or not a remediation plan had been identified yet. The Chair explained that this would be discussed by the IACUC at the next convened meeting. They requested that UCSB submit a written summary describing the potential non-compliance, which was sent to the VMO on May 13, 2019.

On May 17, 2019, the IACUC Chair summarized the incident for the Committee and explained that the USDA had already been notified via the self-reporting process. Prior to discussing corrective actions to be taken by the lab, the Chair explained that, going forward, the lab expects to have fewer and younger animals in the colony as they focus their upcoming work on earlier stages of the disease process. The lab plans to no longer rely on spreadsheet algorithms to identify animals that require enhanced monitoring. The Committee deliberated and outlined multiple corrective actions to be implemented to prevent similar incidents from occurring in the future. First, the lab must label or mark the cage card of all diabetic animals. Next, a second lab member must also review RBG data and ensure that all diabetic animals have been properly identified. Lastly, the lab must send a weekly email report to the IACUC [redacted], informing the [redacted] if any animals began receiving enhanced monitoring procedures that week. The [redacted] will confirm that these animals are euthanized according to the protocol's experimental endpoints. The Committee voted that the corrective actions outlined by the Chair are sufficient and that this incident must be reported to AAALAC. This protocol is not supported by federal funding.

On May 23, 2019, the lab submitted a protocol modification to the IACUC Office to clarify the humane and experimental endpoints, increase the animal numbers for the superovulation project, and include an additional animal procedure (ERG measurements). During the pre-review process, the AV noticed that some of these changes were in conflict with the changes the postdoc proposed during the May 3rd meeting with the sub-Committee. The AV requested that this protocol modification be reviewed by the Committee during a convened meeting.

During the June 12, 2019 IACUC meeting, the AV presented a summary of the proposed changes and how they differ from what had previously been proposed. For example, the lab was now requesting that the experimental endpoint be extended from 10 months of age to 12 months to allow for a potentially larger percentage of the animals to develop diabetic retinopathy. During the May 3rd meeting, the postdoc specifically said that s/he would not be keeping the animals in the colony (i.e., aging) for as long as s/he had been for the current study. The lab has decided to once again include ERG measurements as part of the protocol (the procedure was in a previously approved version of the protocol), which will be performed using animals "[redacted]". Following discussion of the proposed modification, the Committee identified several comments and questions that required clarification from the lab. The Committee voted that the modified protocol should be sent to all members as a request for Designated Member Review prior to approval. In summary, the experimental endpoint was not extended, and the ERG procedure was not added to the protocol. Revisions to the modified protocol were completed and sent to the IACUC for review on July 15, 2019. The modification was approved by Designated Member Review on July 18, 2019.

PROTOCOL (PI being investigated)

Principal Investigator: [redacted]	Phone: N/A
Co-PI:	Phone:
Complete IACUC #: [redacted]	IACUC Title:

	[redacted]
Species/Strain: [redacted] Rat	Current housing location: [redacted]

EVALUATION BY IACUC

☐ No further investigation warranted – Date:_____

☒ Proceed with investigation

☒ Notify Institutional Official

☒ Sub-Committee Appointed: 1. Stu Feinstein

2. Manny Garcia

☒ Report of Investigation (by Sub-Committee to the IACUC) submitted

☒ Convened IACUC meeting review - Date: May 17, 2019

☒ Final IACUC action – Date: May 17, 2019

☒ Notifications required (list): PI, IO, AV, IACUC Chair, [redacted], Postdoc, AAALAC

☒ Notifications sent - Date: PI, IO, AV, IACUC Chair, [redacted], Postdoc (July 30, 2019)