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) 480-3387

May 26, 2020

Re: Animal Welfare Assurance
A3031-01 [OLAW Case 1A]

Dr. Andrew S. Weyrich
Vice President for Research
The University of Utah
(b) (4) Park Building
Salt Lake City, UT 84112

Dear Dr. Weyrich

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your May 7, 2020 letter reporting an adverse event with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Utah (U of U) following up on an initial March 2, 2020 notification by email.

According to the information provided, this Office understands that the U of U Animal Care and Use Committee (ACUC) determined that an adverse event occurred with respect to: the death of an adult marmoset. The final report provides a summary of the event that occurred on February 1, 2020. The summary states an adult marmoset underwent a surgical procedure (bilateral craniotomies and small durotomies) as approved per the protocol on January 29, 2020. No complications occurred during the procedure, the animal recovered well and was left in the incubator overnight. The following day, the Attending Veterinarian (AV) documented post-operative observations of the animal and the treatment plan. On January 31, 2020 the summary states an OCM tech noticed nasal discharge, and treatment was prescribed by the clinical veterinarian. On February 1, 2020 treatment plan was adjusted based on the observations of the animal's lack of appetite, decrease activity level and body temperature. The summary states the animal declined rapidly on February 1st and was euthanized, followed by a necropsy. Following the event, the principal investigator (PI) requested a meeting with the AV, clinical veterinarian, and the PI's lab manager to discuss cause for early termination of the animal. While no definitive cause could be identified, 3 possible causes and potential actions to avoid future recurrence were discussed. They included the following:

- Potential viral infections- Nasal swabs will be taken in all animals that will be anesthetized prior to a procedure to determine whether a viral infection may be present in the colony.

- Stress- Efforts will be made to maintain consistency in the personnel that interacts daily with the animals and improve the training of those people. Factors include minimizing contact with unknown personnel, reducing stress postoperatively and possible hiring of an animal technician by the PI dedicated to taking care of the marmoset colony.

- Drugs- Consideration was given that Alfaxalone may have led to respiratory difficulty when paired with administration of Buprenex. It was discussed that a review of previous records would be done to determine whether other animals administered this same drug combo exhibited respiratory difficulty.

The report states the OCM veterinarian clarified that discussion included concerns by the clinical veterinarians about the ventilator/anesthesia machine setup. It is stated the veterinary staff has been repeatedly concerned about the ventilation of these animals during surgery. It was further clarified that the animal began showing signs of respiratory difficulty/abnormality during the recovery from anesthesia on the day of the procedure. The Institutional Veterinarian stated that in reviewing the history of the last several marmosets, ventilator associated lung injury is a reasonable differential diagnosis and has ordered a new ventilator that is used for marmoset anesthesia by some of the primate centers.

The IACUC discussed the event at the March 26, 2020 convened meeting. A corrective action letter was sent to the PI and at the appeal of the PI the committee again reviewed the events of the matter and additional study related events leading up to the adverse event above and pathology report. Ultimately the IACUC required the following additional actions to be implemented immediately and they include the following:

- A ventilator that is approved by the OCM clinical veterinarian must be used for all surgery/procedures that require anesthesia.

- Surgery procedures that require anesthesia must be scheduled with the OCM clinical veterinarian and must be at a time when veterinary oversight support can be readily available to observe, train and provide study oversight as often the veterinarian deems necessary and must continue for each procedure until the clinical veterinarian is confident of proper equipment function and procedure adherence.

- In consultation with the clinical veterinarian additional sanitation safeguards must be implemented for entry into the IACUC approved surgical suite from the animal facility corridor.

- The IACUC requires surgical progress reports for each animal that includes a description of surgical outcome, animal welfare, and any health status reports on survival surgical studies after recovery.

The report states the IACUC determined the pathology report indicated that endotracheal tissue damage, causing swelling, most likely lead to the early termination of the study animal. The PI stated that recently a change in supplier for the ET tubes had occurred and the outside diameter of the tube was unknowingly larger between suppliers. The size of the ET tube has been corrected per the report.

It is noted that this research is PHS funded. Based on its assessment of this explanation, OLAW understands that the University of Utah has implemented appropriate measures to correct and prevent recurrences of these problems and is now compliant with provisions of the PHS Policy.

We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,
Jacquelyn T. Tubbs -S
Digitally signed by Jacquelyn T. Tubbs -S
Date: 2020.05.27 09:01:12 -04'00'
Jacquelyn T. Tubbs, DVM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact
Robert M. Gibbens, DVM, Director, Animal Welfare Operations

A3031-1A

VICE PRESIDENT FOR RESEARCH
THE UNIVERSITY OF UTAH

May 7, 2020

Brent C. Morse, DVM
Department of Health and Human Services
Rockledge, Suite 360, MSC 7982
Bethesda, MD 20892-7982

Dear Dr. Morse,

Under the provision of IV.F.3 of the Animal Welfare Assurance Policy and as the Institutional Officer at the University of Utah (U of U), I am providing OLAW with a full explanation of circumstances in regard to an adverse event. This was initially reported in a preliminary report emailed to you on March 2, 2020.

Name of Institution: University of Utah
Assurance Number: A3031-01

The following is a brief summary, provided by the investigator, of the potential protocol non-compliance to the IACUC.

1. IACUC approved protocol number: 18-12008
2. Title of protocol: Anatomy, Physiology and Imaging of Visual Cortex in the Non-Human Primate
3. Funding Agency: NSF Grant No. 1755431
4. Animal Species: Marmoset
5. Age of animal: Adult
6. Number of animals involved in the events: 1
7. Date that the event occurred: February 1, 2020
8. Overview of the event (provided by the Principal Investigator and clinical veterinarian):
*The animal underwent a surgical procedure on Jan 29th, which consisted of bilateral craniotomies (one on each side) and small durotomies, followed by intracortical injections of tracer vectors, as per approved IACUC protocol. The procedure went well and was completed around 2:30-3:00pm in the afternoon. The animal recovered well and was left in an incubator overnight. The following day, the attending veterinarian noted "Dizzy recovered well overnight in the incubator. He is very BAR and ate about ¼ of the marmoset porridge. We moved him into a cat carrier where we will offer recovery diet and ensure in a bottle. He also willingly drank about 1.5 ml of ensure from a syringe. We will re-evaluate his appetite in the morning. If it hasn't improved significantly, we'll start cerenia and famotidine for him as well as institute some regular syringe feeding." On the morning of Jan 31st and OCM tech person noticed that the animal had green nasal discharge. Per clinical veterinarian, he was given 0.1ml BenzaPen IM. The following day (Feb 1st) the OCM tech found the animal to be "not very active", lying in the front corner of the carrier, open mouth breathing, and has been eating very little over the past two days. He had a temperature of 98.2*F. Per clinical veterinarian, he was moved back into the incubator this morning. In addition, the following was prescribed through the weekend, 0.03ml Cerenia SQ SID, 0.02ml Famotidine SQ BID if not eating well, syringe fed Ensure BID if not eating well, and will be given 3-5ml 0.9% NACL fluids SQ later today." A few hours later the animal declined rapidly and was euthanized with 1ml of Euthanasia IP, per clinical veterinarian instruction. The clinical veterinarian performed a necropsy later that day and lung tissue was sent for pathology analysis. We have not yet received the results.*
9. Describe the corrective actions to avoid future problems:
After this event Dr Angelucci requested a meeting with the Attending Veterinarian, clinical veterinarian, and Dr. Angelucci' s laboratory manager to discuss possible causes of this animal death. Neither the

veterinarians nor the PI or her staff could not find a definitive cause but we discussed 3 possible causes and potential actions to avoid future similar problems. These are as follows:

a) *Potential viral infections (possibly subclinical and exacerbated by anesthesia).*
Action: we will take nasal swabs in all animals that will be anesthetized prior to a procedure. The goal is to determine whether there may be a viral infection in the colony. One nasal swab was taken by clinical veterinarian on the first animal that underwent a procedure (on 5 Feb 2020) following this meeting.

a. *Stress. Action: we will try to reduce stress in the colony. This will involve: (i) maintaining consistency in the personnel that interacts daily with the animals and improve training of those people; (ii) minimizing contact with unknown personnel (including Angelucci lab) the day of surgery; (iii) reducing stress postoperatively (maybe pairing animals sooner with other colony mates maybe beneficial); (iv) Dr Angelucci discussed the possibility of hiring an animal technician (paid by her) dedicated to taking care of the marmoset colony.*

b. *Drugs. We discussed whether the relatively newly introduced pre-anesthetic drug, Alfaxalone, may somehow lead to postoperative respiratory difficulty when paired with administration of Buprenex. Although the veterinarians did not consider this a likely cause of respiratory problems (as Alfaxalone is deemed to be out of the animal's system by the time Buprenex is administered at the end of the procedure), it was discussed that we will look at pervious records to determine whether other animals that were administered this drug combination showed respiratory difficulty. We did not make any decision to change the current preanesthetic or analgesic plan, but may re-look at this as a possible factor after records have been examined and discussed.*

The OCM clinical veterinarian further clarified that the discussion included concerns by the clinical veterinarians about the ventilator/anesthesia machine set-up, including the concern that we cannot adequately measure tidal volume administered to the animal and peak inspiratory pressure. It was also brought up the possibility that the respiratory issues had a central (nervous system) cause, and were not related to respiratory pathology. The Principal Investigator does not consider these two differentials to be worth discussion, but the veterinary staff has been repeatedly concerned about the ventilation of these animals during surgery. We attempt to manage it when we are in the surgical suite with the lab, but always find that they adjust the ventilation settings to their liking. It was further clarified that the animal began showing signs of respiratory difficulty/abnormality during the recovery from anesthesia on the day of procedure. The Institutional Veterinarian further clarified that looking at the history of the last serval marmosets, ventilator associated lung injury is a reasonable differential diagnosis and has ordered a new ventilator that is used by some of the primate centers for marmoset anesthesia.

The IACUC committee, at the convened meeting on March 26, 2020, discussed the details of the potential protocol adverse event that was provided by the Principal Investigator and sent an IACUC committee corrective action letter to the Principal Investigator that included additional corrective actions. At the appeal of the Principal Investigator the committee again reviewed the events of the adverse event and additional study related events (reported to the IACUC) leading up to the adverse event noted above and pathology report.

The IACUC further discussed the proposed Principal Investigator corrective actions and require the following additional actions to be implemented immediately.

1. Going forward, a ventilator that is approved by the OCM clinical veterinarian must be used for all surgery/procedures that require anesthesia.

2. Surgery procedures that require anesthesia must be scheduled with the OCM clinical veterinarians and must be at a time when veterinary oversight support can be readily available to observe, train, and provide study oversight as often as the veterinarian deems necessary and must continue for each procedure until the clinical veterinarian is confident of proper equipment function and procedure adherence.

3. In consultation with the clinical veterinarian additional sanitation safeguards must be implemented for entry into the IACUC approved surgical suite (b) (4) from the animal facility corridor (i.e., foot bath).

4. The IACUC requires surgical progress reports for each animal that includes a description of surgical outcome, animal welfare, and any health status reports on survival surgical studies after recovery (approximately 7 days post-surgery).

In conclusion the IACUC determined that the animal pathology report indicated that endotracheal tissue damage, causing swelling, most likely lead to the early termination of the study animal. It was further clarified by the Principal Investigator that recently a change in supplier for the endotracheal tubes had been changed (gone out of business) and that the outside diameter of the tube was unknowingly larger between suppliers. The size of the endotracheal tube has been corrected.

The IACUC committee discussed that the death of the marmosets were a serious adverse event and should be reported to the regulatory agency of the Office of Laboratory Animal Welfare (OLAW) and to the USDA.

The IACUC Chair and the IACUC Director discussed the event with the Institutional Official and determined that this was a serious adverse event and that the corrective actions presented by the Principal Investigator and additional corrective actions required by the IACUC were adequate.

Sincerely,

(b) (6)

Andrew Weyrich, Ph.D.
Institutional Official

cc. Robert Gibbens, DVM
Director, Animal Welfare Operations
USDA-APHIS –Animal Care

U of U IACUC Office Files

Walker, Keri (NIH/OD) [C]

From: Morse, Brent (NIH/OD) [E]
Sent: Friday, May 8, 2020 8:13 AM
To: Walker, Keri (NIH/OD) [C]
Cc: Morse, Brent (NIH/OD) [E]
Subject: FW: 18-12008 Protocol Non-Compliance OLAW Letter (University of Utah, 05/07/2020)
Attachments: 18-12008 Protocol Non-Compliance OLAW Letter_Final.pdf

Follow Up Flag: Follow up
Flag Status: Completed

Hi Keri,

Please use this email and the attached letter to open a case file. Put the file folder in my mailbox and I will work on a response. Thank you. Brent

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

From: Morse, Brent (NIH/OD) [E]
Sent: Friday, May 08, 2020 8:11 AM
To: Andrew S Weyrich <andy.weyrich@utah.edu>; iacuc@ocm.utah.edu
Cc: Steven Dickman <Sdickman@ocm.utah.edu>
Subject: RE: 18-12008 Protocol Non-Compliance OLAW Letter (University of Utah, 05/07/2020)

Thank you for this report Dr. Weyrich. We will send an official response soon.

Sincerely, Brent Morse

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

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

From: [redacted] (b) (6) **On Behalf Of** Andrew S Weyrich
Sent: Thursday, May 07, 2020 2:39 PM
To: Morse, Brent (NIH/OD) [E] <morseb@mail.nih.gov>; robert.m.gibbens@usda.gov; iacuc@ocm.utah.edu

Cc: Steven Dickman <Sdickman@ocm.utah.edu>
Subject: 18-12008 Protocol Non-Compliance OLAW Letter (University of Utah, 05/07/2020)

May 7, 2020

Brent C. Morse, DVM
Department of Health and Human Services
Rockledge, Suite 360, MSC 7982
Bethesda, MD 20892-7982

Dear Dr. Morse,

Under the provision of IV.F.3 of the Animal Welfare Assurance Policy and as the Institutional Officer at the University of Utah (U of U), I am providing OLAW with a full explanation of circumstances in regard to an adverse event, (see attached and below). This was initially reported in a preliminary report emailed to you on March 2, 2020.

Name of Institution: University of Utah
Assurance Number: A3031-01

The following is a brief summary, provided by the investigator, of the potential protocol non-compliance to the IACUC.

1. IACUC approved protocol number: 18-12008

2. Title of protocol: Anatomy, Physiology and Imaging of Visual Cortex in the Non-Human Primate

3. Funding Agency: NSF Grant No. 1755431

4. Animal Species: Marmoset

5. Age of animal: Adult

6. Number of animals involved in the events: 1

7. Date that the event occurred: February 1, 2020

8. Overview of the event (provided by the Principal Investigator and clinical veterinarian):
*The animal underwent a surgical procedure on Jan 29th, which consisted of bilateral craniotomies (one on each side) and small durotomies, followed by intracortical injections of tracer vectors, as per approved IACUC protocol. The procedure went well and was completed around 2:30-3:00pm in the afternoon. The animal recovered well and was left in an incubator overnight. The following day, the attending veterinarian noted "Dizzy recovered well overnight in the incubator. He is very BAR and ate about ¼ of the marmoset porridge. We moved him into a cat carrier where we will offer recovery diet and ensure in a bottle. He also willingly drank about 1.5 ml of ensure from a syringe. We will re-evaluate his appetite in the morning. If it hasn't improved significantly, we'll start cerenia and famotidine for him as well as institute some regular syringe feeding." On the morning of Jan 31st and OCM tech person noticed that the animal had green nasal discharge. Per clinical veterinarian, he was given 0.1ml BenzaPen IM. The following day (Feb 1st) the OCM tech found the animal to be "not very active", lying in the front corner of the carrier, open mouth breathing, and has been eating very little over the past two days. He had a temperature of 98.2*F. Per clinical veterinarian, he was moved back into the incubator this morning. In addition, the following was prescribed through the weekend, 0.03ml Cerenia SQ SID, 0.02ml Famotidine SQ BID if not eating well, syringe fed Ensure BID if not eating well, and will be given 3-5ml 0.9% NACL fluids SQ later today." A few hours later the animal declined rapidly and was euthanized with 1ml of Euthanasia IP, per clinical*

veterinarian instruction. The clinical veterinarian performed a necropsy later that day and lung tissue was sent for pathology analysis. We have not yet received the results.

9. Describe the corrective actions to avoid future problems:
After this event Dr Angelucci requested a meeting with the Attending Veterinarian, clinical veterinarian, and Dr. Angelucci' s laboratory manager to discuss possible causes of this animal death. Neither the

veterinarians nor the PI or her staff could not find a definitive cause but we discussed 3 possible causes and potential actions to avoid future similar problems. These are as follows:

a) *Potential viral infections (possibly subclinical and exacerbated by anesthesia).*
Action: we will take nasal swabs in all animals that will be anesthetized prior to a procedure. The goal is to determine whether there may be a viral infection in the colony. One nasal swab was taken by clinical veterinarian on the first animal that underwent a procedure (on 5 Feb 2020) following this meeting.

a. *Stress. Action: we will try to reduce stress in the colony. This will involve: (i) maintaining consistency in the personnel that interacts daily with the animals and improve training of those people; (ii) minimizing contact with unknown personnel (including Angelucci lab) the day of surgery; (iii) reducing stress postoperatively (maybe pairing animals sooner with other colony mates maybe beneficial); (iv) Dr Angelucci discussed the possibility of hiring an animal technician (paid by her) dedicated to taking care of the marmoset colony.*

b. *Drugs. We discussed whether the relatively newly introduced pre-anesthetic drug, Alfaxalone, may somehow lead to postoperative respiratory difficulty when paired with administration of Buprenex. Although the veterinarians did not consider this a likely cause of respiratory problems (as Alfaxalone is deemed to be out of the animal's system by the time Buprenex is administered at the end of the procedure), it was discussed that we will look at pervious records to determine whether other animals that were administered this drug combination showed respiratory difficulty. We did not make any decision to change the current preanesthetic or analgesic plan, but may re-look at this as a possible factor after records have been examined and discussed.*

The OCM clinical veterinarian further clarified that the discussion included concerns by the clinical veterinarians about the ventilator/anesthesia machine set-up, including the concern that we cannot adequately measure tidal volume administered to the animal and peak inspiratory pressure. It was also brought up the possibility that the respiratory issues had a central (nervous system) cause, and were not related to respiratory pathology. The Principal Investigator does not consider these two differentials to be worth discussion, but the veterinary staff has been repeatedly concerned about the ventilation of these animals during surgery. We attempt to manage it when we are in the surgical suite with the lab, but always find that they adjust the ventilation settings to their liking. It was further clarified that the animal began showing signs of respiratory difficulty/abnormality during the recovery from anesthesia on the day of procedure. The Institutional Veterinarian further clarified that looking at the history of the last serval marmosets, ventilator associated lung injury is a reasonable differential diagnosis and has ordered a new ventilator that is used by some of the primate centers for marmoset anesthesia.

The IACUC committee, at the convened meeting on March 26, 2020, discussed the details of the potential protocol adverse event that was provided by the Principal Investigator and sent an IACUC committee corrective action letter to the Principal Investigator that included additional corrective actions. At the appeal of the Principal Investigator the committee again reviewed the events of the adverse event and additional study related events (reported to the IACUC) leading up to the adverse event noted above and pathology report.

The IACUC further discussed the proposed Principal Investigator corrective actions and require the following additional actions to be implemented immediately.

1. Going forward, a ventilator that is approved by the OCM clinical veterinarian must be used for all surgery/procedures that require anesthesia.

2. Surgery procedures that require anesthesia must be scheduled with the OCM clinical veterinarians and must be at a time when veterinary oversight support can be readily available to observe, train, and provide study oversight as often as the veterinarian deems necessary and must continue for each procedure until the clinical veterinarian is confident of proper equipment function and procedure adherence.

3. In consultation with the clinical veterinarian additional sanitation safeguards must be implemented for entry into the IACUC approved surgical suite (b) (4) from the animal facility corridor (i.e., foot bath).

4. The IACUC requires surgical progress reports for each animal that includes a description of surgical outcome, animal welfare, and any health status reports on survival surgical studies after recovery (approximately 7 days post-surgery).

In conclusion, the IACUC confirmed the animal pathology report indicated that endotracheal tissue damage, causing swelling, most likely lead to the early termination of the study animal. It was further clarified by the Principal Investigator that recently a change in supplier for the endotracheal tubes had been changed (gone out of business) and that the outside diameter of the tube was unknowingly larger between suppliers. The size of the endotracheal tube has been corrected.

The IACUC committee discussed that the death of the marmosets were a serious adverse event and should be reported to the regulatory agency of the Office of Laboratory Animal Welfare (OLAW) and to the USDA.

The IACUC Chair and the IACUC Director discussed the event with the Institutional Official and determined that this was a serious adverse event and that the corrective actions presented by the Principal Investigator and additional corrective actions required by the IACUC were adequate.

Sincerely,

Andrew Weyrich, Ph.D.
Institutional Official

Andrew S. Weyrich, Ph.D.
Vice President for Research
Professor of Internal Medicine
The University of Utah
P: (b) (6)

Please contact (b) (6) for scheduling requests, including events and presentations.

A3031-1A

Tubbs, Jai (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, March 2, 2020 2:16 PM
To: Steven Dickman; OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Preliminary report to OLAW A3031-01

Hello Mr. Dickman,

Thank you for the preliminary report. We will open a case file and await the final report.

Kind Regards,

Jacquelyn Tubbs, DVM, DACLAM
Veterinary Medical Officer
Office of Laboratory Animal Welfare
National Institutes of Health

From: Steven Dickman <Sdickman@ocm.utah.edu>
Sent: Monday, March 2, 2020 1:04 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: FW: Preliminary report to OLAW A3031-01

As per auto-instructions I am forwarding this preliminary report.

From: Steven Dickman
Sent: Monday, March 2, 2020 10:58 AM
To: morseb@mail.nih.gov
Subject: Preliminary report to OLAW A3031-01

Dr. Morse,

I have attached a copy of a preliminary report to OLAW concerning the death of a marmoset monkey. We will follow up timely.

Thanks for your help.

Steven Dickman
IACUC Director
University of Utah

THE UNIVERSITY OF UTAH

Preliminary Report

March 2, 2020

Name and Contact Information of Person Reporting

Derek Dosdall
IACUC Chair
University of Utah
iacuc@ocm.utah.edu
(b) (6)

Name of Institution

University of Utah

Assurance Number

A3031-01

Funding component and if contacted

NSF Grant No. 1755431 – not contacted

Brief Description of Incident

Dates:	February 1, 2020
Personnel:	Principal Investigator and staff
Species:	Marmoset
Description:	The animal underwent a surgical procedure on Jan 29th, which consisted of bilateral craniotomies (one on each side) and small durotomies, followed by intracortical injections of tracer vectors, as per approved IACUC protocol. The procedure went well and was completed around 2:30-3:00pm in the afternoon. The animal recovered well and was left in an incubator overnight. The following day, the attending veterinarian noted "Dizzy recovered well overnight in the incubator. He is very BAR and ate about ¼ of the marmoset porridge. We moved him into a cat carrier where we will offer recovery diet and ensure in a bottle. He also willingly drank about 1.5 ml of ensure from a syringe. We will re-evaluate his appetite in the morning. If it hasn't improved significantly, we'll start cerenia and famotidine for him as well as institute some regular syringe feeding." On the morning of Jan 31st and OCM tech person noticed that the animal had green nasal discharge. Per clinical veterinarian, he was given 0.1ml BenzaPen IM. The following day (Feb 1st) the OCM tech found the animal to be "not very active", lying in the front corner of the carrier, open mouth breathing, and has been eating very little over the past two days. He had a temperature of 98.2*F. Per clinical veterinarian, he was moved back into the incubator this morning. In addition, the following was prescribed through the weekend, 0.03ml Cerenia SQ SID, 0.02ml Famotidine SQ BID if not eating well, syringe fed Ensure BID if not eating well, and will be given 3-5ml 0.9% NACL fluids SQ later today." A few hours later the animal declined rapidly and was euthanized with 1ml of Euthanasia IP, per clinical veterinarian instruction. The clinical veterinarian performed a necropsy later that day and lung tissue was sent for pathology analysis. We have not yet received the results.

Plan and schedule for correction and prevention (if known)

The IACUC met at a convened IACUC meeting (February 26, 2020) and discussed corrective actions which included the following:

Described by the Principal Investigator –

a) *Potential viral infections (possibly subclinical and exacerbated by anesthesia). Action: we will take nasal swabs in all animals that will be anesthetized prior to a procedure. The goal is to determine whether there may be a viral infection in the colony. One nasal swab was taken by clinical veterinarian on the first animal that underwent a procedure (on 5 Feb 2020) following this meeting.*

a. *Stress. Action: we will try to reduce stress in the colony. This will involve: (i) maintaining consistency in the personnel that interacts daily with the animals and improve training of those people; (ii) minimizing contact with unknown personnel (including Angelucci lab) the day of surgery; (iii) reducing stress postoperatively (maybe pairing animals sooner with other colony mates maybe beneficial); (iv) Dr Angelucci discussed the possibility of hiring an animal technician (paid by her) dedicated to taking care of the marmoset colony.*

b. *Drugs. We discussed whether the relatively newly introduced pre-anesthetic drug, Alfaxalone, may somehow lead to postoperative respiratory difficulty when paired with administration of Buprenex. Although the veterinarians did not consider this a likely cause of respiratory problems (as Alfaxalone is deemed to be out of the animal's system by the time Buprenex is administered at the end of the procedure), it was discussed that we will look at pervious records to determine whether other animals that were administered this drug combination showed respiratory difficulty. We did not make any decision to change the current preanesthetic or analgesic plan, but may re-look at this as a possible factor after records have been examined and discussed.*

Additional Corrective Action required by the IACUC:

a) Going forward a replacement ventilator, provided by the Comparative Medicine Center and approved by the OCM clinical veterinarian, must be used on all surgery/procedures that require anesthesia.
b) Surgery/procedures that require anesthesia must be scheduled with the OCM clinical veterinarians and must be at a time when clinical support can be provided by the veterinarian or veterinarian OCM approved personnel to maintain anesthesia throughout the entire surgery/procedure.
c) Recovery surgery must be completed in the designated OCM operating room.
d) The IACUC requires surgical progress reports for each animal that includes a description of surgical outcome, animal welfare, and any health status reports on survival surgical studies after recovery (approximately 7 days post-surgery).
e) The committee wants to clarify that known pregnant animals should not be enrolled in approved study procedures that require surgery.

The IACUC Director and chair met with the Institutional Officer to review and report the adverse event to OLAW through the IO. However, the Principal Investigator has requested to provide additional information and alternative solutions for corrective actions. The Institutional Officer decided to have the IACUC send a preliminary report to OLAW and allow the Principal Investigator to provide additional information before sending the final report by the IO.

Timeframe for final report from the Institutional Official

The Institutional Official has already been notified of the adverse event by the IACUC Chair. The IACUC is scheduled to hold a convened IACUC meeting on March 25th and provide time for the Principal Investigator to present additional information and alternatives to required corrective action for reconsideration. A final report to OLAW will be submitted timely after that meeting (first of April 2020).

IACUC Department
Phone: (801) 581-5950
Email: iacuc@ocm.utah.edu