DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:
Office of Laboratory Animal Welfare
6700B Rockledge Drive
Suite 2500, MSC 6910
Bethesda, Maryland 20892-6910
Home Page: http://grants.nih.gov/grants/olaw/olaw.htm

FOR EXPRESS MAIL:
Office of Laboratory Animal Welfare
6700B Rockledge Drive
Suite 2500
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

September 29, 2021

Re: Animal Welfare Assurance
#A3234-01 (OLAW Case H)

Dr. Shaban Demirel
Interim Vice President of Research
Legacy Health System
1225 NE 2nd Avenue
Portland, Oregon 97232

Dear Dr. Demirel,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of the September 24, 2021 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Legacy Research Institute. According to the information provided, OLAW understands that a nonhuman primate died while attached to an anesthesia machine because the pop-off valve had been left closed after initial testing of the circuit. If not corrected quickly, this causes pressure in the breathing circuit and lungs, damage to the lungs, pneumothorax, and death.

The immediate action taken upon discovery consisted of resuscitation attempts, which were unsuccessful due to the length of time that had passed. The veterinary technician responsible was retrained on all of the steps involved in testing the anesthetic machine and on monitoring the animal. The research staff agreed to also assist in monitoring. The Attending Veterinarian has ordered a pop-off safety valve for the large animal anesthesia machines and this device may contribute to prevention of a future incident. The technician involved has left the institution and all other technicians have been retrained on anesthetic procedures and monitoring.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to prevent recurrence of this problem. OLAW concurs with the actions taken by the institution to comply with the PHS Policy. Please ensure that future noncompliance reports are signed by the Institutional Official, identify the source of funding for the project involved, and provide the relevant grant number(s) if PHS-supported. Thank you for keeping OLAW apprised on this matter.

Sincerely,

(b) (6)

Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare

cc: IACUC Chair
Paul Newton, JD, Senior Research Regulatory Specialist
Robert Gibbens, D.V.M., USDA-APHIS-AC

A 3234-H

LEGACY HEALTH

LEGACY RESEARCH INSTITUTE
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE

Submit completed forms to:
(b) (6)
(b) (6)

ADVERSE EVENTS, UNEXPECTED OUTCOMES, PROTOCOL DEVIATION FORM

IACUC Chair:
Brad Fortune, PhD (b) (6) | bfortune@deverseye.org
Attending Veterinarian:
Jennifer Wilk, DVM, DACLAM (b) (6) | jenwilk@lhs.org

Date of form completion: 9/10/2021
Protocol #: 112-2020 **PI:** Fortune
Protocol Title: Early-stage axon damage: active transport and cytoskeletal ultrastructure within individual axons of glaucomatous non-human primate eyes
Person completing form if not PI: Jennifer Wilk (AV)

Date of AE/UO/PD: 9/9/2021 Date Identified: 9/9/2021
Event: Adverse Event

Is the possibility of this event listed in the current protocol? ☐ Yes ☐ No X N/A

Nature of Event – please describe what happened:
On 9/9/21, a nonhuman primate (NHP) was anesthetized for a scheduled project procedure under this protocol. As is customary, a DCM technician was managing the anesthesia. The technician is a Certified Veterinary Technician. After the NHP was transported from the vivarium to the procedure room (307), the lab staff proceeded to prep the NHP and equipment for the procedure, while the DCM tech worked on setting up all of the anesthesia support components. This includes hooking the animal up to the anesthesia machine in the room, setting the rate for anesthetic gas delivery, setting the rates for medical air and oxygen delivery, connecting the end tidal CO2 monitor, attachment of the sensors for oxygenation saturation levels and body temperature, connecting the ECG leads to the animal, placing a blood pressure cuff, starting 2 different types of IV fluids (1 colloid and 1 crystalloid), and applying warming devices to the NHP. Once everything is properly set-up and confirmed to be operating correctly, a baseline collection of vital statistics is recorded by both DCM and the research staff, followed by subsequent periodic recordings every 15 minutes.

Part of standard equipment set-up for the day includes a 10-second test of the anesthesia machine. The purpose of this test is to confirm integrity of the breathing circuit. During the test, the adjustable pressure limit (aka 'pop-off') valve is closed, the outflow for the circuit (i.e. the animal end) is occluded, the circuit is pressurized via addition of gas using the oxygen flush valve. Once the circuit is pressurized, the anesthetic vaporizer is turned on and off, and the pressure valve is monitored for

stability. If the pressure drops during any portion of the 10-second test, there is a leak in the breathing circuit which must be rectified before anesthesia is initiated. After the check is complete, the pop-off valve must be opened both to depressurize the circuit and to ensure proper function of the anesthesia machine.

However, in this instance, during animal set-up, the pulse oximeter was not functioning properly so the DCM tech was spending extra time concentrating on this step. The research technician commented that the NHP's nostrils were flaring under anesthesia, which is unusual. The DCM tech then looked at the physiologic monitor to evaluate the parameters and noticed that there were no end-tidal CO2 wave forms being recorded. As this monitor was in place and had been working correctly initially, this is indicative of arrested respiration. The DCM tech then observed that the anesthesia reservoir bag and the NHP's chest were maximally distended. The DCM tech realized they had forgotten to open the pop-off valve after the 10-second test of the anesthesia machine that morning.

Describe the initial actions taken to manage the situation:
The DCM tech immediately opened the pop-off valve, and checked for a pulse. The DCM tech visually confirmed that the animal was not breathing, but could palpate a weak and slow pulse. CPR was initiated immediately and the DCM tech called for back-up assistance. Resuscitation was not successful.

The result of a closed pop-off valve is build-up of pressure within the breathing circuit, and ultimately the animal's lungs. The DCM tech estimated the NHP had been connected to the breathing circuit for 5-10 minutes before the complications were observed. During this time, oxygen, medical air and vaporized anesthetic were being delivered to the animal without a pressure relief outlet. Even in this short time, the pressure builds to the point that pulmonary barotrauma occurs, then rupture of the alveolar sacs. Once the alveolar sacs rupture, pneumothorax develops as the air flows through the now-ruptured lungs into the chest cavity. Death is nearly instant following alveolar sac rupture, and no amount of CPR would have been successful.

Describe actions taken to prevent this type of event in the future:
Multiple debriefing meetings occurred that day between the AV and the DCM tech, and the AV and the research staff. The DCM tech is aware that their mistake in missing this critical step during the anesthesia machine test was directly responsible for the NHP's death. The tech was retrained on the steps for the 10-second anesthesia machine test, as well as the importance of keeping eyes on the animal and vital parameters at all times, even when performing other activities and in-between the timepoints for recording vitals. Earlier observation of the increasing distention of the reservoir bag, changes in character of respirations, elevation of end-tidal CO2 levels, decrease of oxygen saturation levels, and/or evaluation of the breathing circuit's pressure readings might have saved this NHP. The research staff indicated they would contribute to animal monitoring by keeping an eye on the reservoir bag as well.

In addition, pop-off occlusion valves are available which can protect against most pop-off valve related accidents. The AV has already contacted the anesthesia equipment service technician to order these safety valves for installation on all large animal anesthesia machines.

As a side note, the DCM technician involved with this incident had already accepted another position at veterinary hospital and given 2 weeks' notice (their last scheduled day is 9/11/21). Although the tech responsible for the error will no longer be with DCM, the other DCM techs who administer anesthesia are receiving refresher training about the importance of following all procedural steps.

Walker, Keri (NIH/OD) [E]

From: (b) (6)
Sent: Friday, September 24, 2021 2:00 PM
To: OLAW Division of Compliance Oversight (NIH/OD); Wolff, Axel (NIH/OD) [E]
Cc: Demirel, Shaban :LRI VP Interim; Fortune, Brad :LRI Research; Wilk, Jennifer L :LRI Dir Comparative Medicine
Subject: reportable incident
Attachments: LRI 112-2020 Adverse Event Report.pdf

Follow Up Flag: Follow up
Flag Status: Flagged

To:
Axel Wolfe, MS, DVM
Deputy Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

Dear Dr. Wolfe:

I am the regulatory compliance specialist and IACUC Administrator for Legacy Research Institute (LRI). Dr. Shaban Demirel is the Institutional Official for LRI. Dr. Brad Fortune is the IACUC Chair and Dr. Jennifer Wilk is the Attending Vet at LRI.

I have left you a phone message regarding this reportable incident this morning and wanted to provide additional details.

Please find attached a report of a reportable incident at Legacy Research Institute. We believe that this incident falls under the category noted in Notice Number: NOT-OD-05-034 of a reportable incident: "conditions that jeopardize the health or well-being of animals, including natural disasters, accidents, and mechanical failures, resulting in actual harm or death to animals."

The incident involves the death of a nonhuman primate undergoing procedures for an IACUC approved study. The death was caused by human error.

The adverse event report was reviewed and acknowledged by the Legacy IACUC on September 16, 2021. Legacy Research Institute is continuing to work through the ramifications of this incident.

Please contact me at your earliest convenience.

Thank you,

(b) (6)

(b) (6)

Walker, Keri (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, September 27, 2021 9:19 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: reportable incident

On behalf of Dr. Wolff, I am responding to your voicemail and this report. You are correct in categorizing this incident as the first bullet in reporting requirements. As this was a preventable human error, it could also be related to bullet three. We will respond to the IO in reference to this report shortly.

Thank you,
Keri

Keri Walker
Program Analyst
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
6700B Rockledge Dr., Suite 2500
Bethesda, MD 20892
301-435-2390
keri.walker@nih.gov

From: (b) (6)
Sent: Friday, September 24, 2021 2:00 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>; Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>
Cc: Demirel, Shaban :LRI VP Interim <SDEMIREL@LHS.ORG>; Fortune, Brad :LRI Research <bfortune@deverseye.org>; Wilk, Jennifer L :LRI Dir Comparative Medicine <JENWILK@lhs.org>
Subject: reportable incident

To:
Axel Wolfe, MS, DVM
Deputy Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

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