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

July 18, 2018

Re: Animal Welfare Assurance
A4614-01 [OLAW Case M]

Dr. Gregory Kelly
Senior Vice President
SoBran, Inc.
4000 Blackburn Lane, (b) (4)
Burtonsville, MD 20866

Dear Dr. Kelly,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of a letter dated June 22, 2018 reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Sobran BioScience.. According to the information provided, OLAW understands that two cats died as the result of anesthetic complications associated with the use of a new V-gel device and exacerbated by a piece of equipment associated with the experiment. Due to the positioning of the head and neck required for the experiment, the V-gel device may have reduced the flow of oxygen into the trachea and the equipment covered most of the cat's body which prevented normal monitoring of respiration and oxygenation. These factors coupled with inconsistent pulse oximetry resulted in the two deaths. The large size of the animals also appeared to be a factor. It was stated that the animals were not funded by the PHS.

Corrective actions included changing to a regimen of injectable anesthesia which was used on four animals without complication. Possible preventive measures include the use of a traditional endotracheal tube if injectable anesthesia is not used, although this would be expected to cause issues due to the positioning of the head and neck, and modification of the piece of experimental equipment to allow better visualization of the cat and minimize the required rotation of the cat's head.

OLAW believes that the corrective and preventative measures put in place by Sobran BioScience are consistent with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals. Although this activity was not PHS funded, the application of the standards of the PHS Policy across the animal care and use program reduces any potential appearance of a double standard. For future reports, please sign or initial the report as the Institutional Official responsible for reporting. Thank you. We appreciate being informed of this incident and find no cause for further action by this office.

Sincerely,

(b) (6)

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

cc: IACUC Contact
Dr. Robert M. Gibbens, USDA, APHIS, AC

A4614 - M

Rangos Facility
SoBran, Inc.
855 N. Wolfe St.
Baltimore, MD 21205
22 June, 2018

Thru: Institutional Official, SoBran, Incorporated, Blackwell Lane, Burtonsville, MD

For: Office of Laboratory Animal Welfare (OLAW), Division of Compliance Oversight (DCO), National Institutes of Health, Bethesda, MD, olawdco@mail.nih.gov

SUBJECT: Animal Protocol Adverse Event – Unexpected Cat Mortality During V-Gel Use

1. This memorandum describes unexpected animal deaths occurring during conduct of a recent experiment. Two cats died; no protocol or PHS noncompliance was found to occur related to these events.

2. Background and key points:

   a. This is not a PHS-funded study. The events described below occurred on15 May 2018 and were discussed at the 22 June 2018 IACUC meeting.

   b. Cats were to be anesthetized for 80-90 minutes total. A new anesthesia method was to be used, as determined by the previous clinical veterinarian who has since left the facility. The equipment to be used was the V-gel inhalant anesthetic device. This device sits over the trachea opening rather than entering the trachea, and thus appeared to be a good refinement because there is no potential intratracheal trauma; a traditional endotracheal tube sits inside the trachea and can cause post-procedure complications due to swelling. Prior to the event the Attending Veterinarian and clinical veterinarian familiarized themselves with the device placement. The V-gel device was to be used for 8 cats during this experiment. On Day 1, cat 1 was anesthetized using the device. The experimental manipulation required rotating the animal's head approximately greater than 90 degrees to the left and then also tilted backwards towards the tabletop, while a large device that covered the animal's head, thorax and part of its abdomen was placed over it. During this manipulation, during pulse oximetry was nonfunctional, the animal went into respiratory arrest and was unable to be resuscitated. The second and third animals were manipulated in the same way and completed the procedure without incident. The fourth animal experienced the same signs as the first animal and died.

   c. An immediate after-action review held after completion of 4th animal found the following factors as possibly contributing to animal death:

      - Inability to quickly identify animal distress due to lack of consistent pulse oximeter readings, inability to see animal head, thorax and part of abdomen, and inability to see animal's mucous membranes.

- Both animal's that died were significantly larger than the other two animals that survived, by 2-3 kg.

d. Based on the events and factors discussed, the following was proposed as possible cause of animal death:

- General V-gel incompatibility with the procedure at hand. Due to the twisting of the head in two dimensions, and this twisting being inconsistant between animals (since scientists are still developing their procedure), the V-gel may have shifted off the trachea entrance.
- Specific V-gel factors contributing to tracheal blockage. The device is bulky along its edges, unlike a traditional endotracheal tube; shifting of the device off the trachea entrance could have (paradoxically) led to partial tracheal blockage. Partial tracheal blockage would not manifest as immediate distress but as a gradual loss of oxygenation. Without ability to see head, mucous membranes, and thorax, and lack of consistent pulse oximetry levels, detecting this gradual loss of oxygen saturation would be difficult until it was at a critical stage and animal went into distress.
- V-gel size relative to cat size. Since the two animals surviving were significantly smaller than the two animals that did not survive, sizing of the V-gel may need to be more precise to avoid any slippage and resultant blockage of trachea described above.

e. Pathology assessment of animals was not done as the animal head and other tissues were needed for experimental purposes.

3. Plan for Correction and Reporting:

1) Plan for correction – change in procedures.

a. The remaining four cats were anesthetized with injectable anesthetic without incident. This will continue, or a traditional ET tube will be used, though it is expected that the ET tube will not be compatible with the magnet-holding device covering the animal nor the required head rotation in two planes.

b. The PI brought their biomedical engineer to observe the second day's proceedings (cats #5-8). They wanted to identify how they could redesign their magnet device to allow for better visualization of the animal head as well as minimize the required rotation of the animal's head for their procedures.

2) Reporting – The IO was notified on 16 May 2018 and the event discussed at the June 2018 IACUC meeting.

4. Point of contact is the undersigned at mobile (b) (6) or email aschiavetta@sobran-inc.com.

Ann M. Schiavetta
DVM, MS, DACLAM
Chair, Rangos IACUC

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, July 16, 2018 8:35 AM
To: Ann Schiavetta; OLAW Division of Compliance Oversight (NIH/OD)
Cc: Greg Kelly
Subject: RE: Adverse Event Report - SoBran Rangos Facility

Thank you for this information Dr. Schiavetta. We will send an official response soon.

Best regards, Brent Morse

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

From: Ann Schiavetta [mailto:ASchiavetta@sobran-inc.com]
Sent: Monday, July 16, 2018 8:05 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Greg Kelly <GKelly@sobran-inc.com>
Subject: Adverse Event Report - SoBran Rangos Facility

Good morning,

Please find attached report of adverse event.

This was discussed with the IO the day after the event, and at a follow-on meeting, as well as at a following IACUC meeting.

V/r,

Ann M. Schiavetta
DVM, MS, DACLAM
SoBran, Inc.
Academic / Commercial Division
Chair, IACUC, SoBran Commercial Facilities
email: aschiavetta@sobran-inc.com
mobile: (b) (6)

from your computer. Thank you.

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