



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

June 25, 2021

Re: Animal Welfare Assurance
A3377-01 [OLAW Case 8O]

Dr. David P. Norton
Vice President for Research
University of Florida
(b) (4) Grinter Hall
Gainesville, FL 32611-5500

Dear Dr. Norton,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your June 2, 2021 letter reporting an adverse event at the University of Florida. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, this Office understands that the University of Florida Animal Care and Use Committee (ACUC) determined that an adverse event occurred with respect to: the development of wound dehiscence and infections at the limb surgical sites in rats. The final report states between March 24-25, 2021, a surgical procedure was performed in 13 rats per the IACUC protocol. On March 29, 2021, wound dehiscence and redness were observed in one rat, and euthanasia was recommended by the on-call veterinarian. The following day purulent discharge and an abscess was observed in one rat, which was subsequently euthanized, while another rat received antibiotics due to signs of infection. Ultimately, 11 additional animals were administered antibiotics and additional post-operative pain management due to suspected lack of wound healing, and the veterinary recommendations included wound cleaning as well. Per the report, all animals improved with the ongoing treatment.

The IACUC full committee voted the matter as an adverse event on May 4, 2021. It is understood the principal investigator and all surgeons/assistants have been working with the ACS veterinarian to identify the root cause of these findings. The report states a review of the sterile material used, how it was prepped, and the aseptic approach utilized for the limb incision is ongoing. The following summary includes the sources identified as potential contributors to these findings and subsequent corrective actions:

- Regarding PBS (sterile) used for the limb procedure, separate bottles of sterile saline were used for the cervical and limb incisions. Both solutions were similar in appearance and were deemed to be free of any visible contaminants, although potential microbiological contamination was not assessed by culture.
- Corrective action: an unopened bottle of sterile saline will be used for each incision in future surgeries.
- Suturing technique used to close the limb incision involved the use of interrupted sutures. The suture pattern may encourage the animal to pick out their sutures through biting/digging contributing to wound reopening, increased inflammation, and infection.
- Corrective action: the lab will use a continuous suturing technique for future limb incisions.

- Lack of aseptically re-prepping the limb after transferring from one sterile field to another- both regions were prepped using aseptic technique before transfer to a sterile field for subsequent surgery.
- Corrective action: it will now be re-prepped by applying 3 rounds of betadine and ethanol again after the vagotomy procure.
- The surgical drape will be cut to fit the limb more snugly and limit contamination even further.
- The surgical tools used for each animal will be logged.

It is understood that this project is supported by PHS funds. OLAW assumes the IACUC has verified additional training of personnel on the protocol was not necessary. Based on its assessment of this explanation, OLAW understands that the University of Florida has implemented appropriate measures to correct and prevent recurrences of these problems.

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

Sincerely,
Jacquelyn T.
Tubbs -S
Jacquelyn Tubbs, DVM, DACLAM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

Digitally signed by Jacquelyn
T. Tubbs -S
Date: 2021.06.25 11:34:27
-04'00'

cc: IACUC Contact



Office of the Vice President for Research

223 Grinter Hall
PO Box 115500
Gainesville, FL 32611-5500
352-392-1582
352-392-9605 Fax

June 2, 2021

Axel Wolff, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360
6705 Rockledge Drive
Bethesda, MD 20892

Dear Dr. Wolff:

The University of Florida, in accordance with Assurance D16-00244 (A3377-01) and PHS Policy IV.F.3., provides this report of an adverse event regarding rats that developed wound dehiscence and infections at the limb surgical site. A preliminary report was not sent regarding this adverse event.

On 3/24/2021 and 3/25/2021, medial meniscus transection on the right hind limb and left cervical vagotomy was performed in 13 rats per the IACUC protocol.

- On the evening of 03/29/2021 wound dehiscence and redness in one rat's limb was noted, the on-call vet was notified and euthanasia was recommended. Two additional rats had redness and skin thickening along the incision site.
- A vet consultation occurred on 3/30/2021. One rat had purulent discharge and an abscess in the vagotomy site, and that animal was euthanized. Another was placed on antibiotics due to evidence of infection.
- Due to the redness and lack of wound healing suspected in 11 other animals, following vet consultation, all rats were placed on antibiotics (Baytril antibiotic water) and additional post-operative pain management (meloxicam). The vet also recommended that the animal's wounds be thoroughly cleaned using chlorohexidine which was performed that same evening (03/30).
- All animals improved with the ongoing treatment.

The IACUC full committee voted on May 4, 2021 that this incident was an adverse event. The laboratory has implemented the following corrective actions:

1. The PI and all surgeons/assistants have been working with an ACS veterinarian to identify the root cause of this adverse event. A thorough review of the sterile material used, how it was prepped, and the aseptic approach utilized for the limb incision is ongoing. The lab has identified the following sources as potential contributors to this adverse event:

Report of an adverse event

June 2, 2021

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- a. PBS (sterile) used for the limb procedure- separate bottles of sterile saline were used for the cervical and limb incisions. Due to this, a sample of the saline solution used for the limb incision was inspected under a microscope and compared to the saline used for the cervical incision. Both of these solutions were similar in appearance and were deemed to be free of any visible contaminants, although potential microbiological contamination was not assessed by culture. Regardless, an unopened bottle of sterile saline will be used for each incision in future surgeries.
- b. Suturing technique used to close the limb incision- the technique for limb incision involved interrupted sutures. That leaves more material at the incision site and may encourage the animal to pick out their sutures through biting/digging contributing to wound reopening, increased inflammation, and infection. To mitigate, the lab will use a continuous suturing technique for future limb incisions.
- c. Lack of aseptically re-prepping the limb after transferring from one sterile field to another- both regions were prepped using aseptic technique (3 rounds of betadine and ethanol to both sites) before transfer to a sterile field for subsequent surgery. Because the limb may contact a towel (although sterile) during the first procedure, it will now be re-prepped by applying 3 rounds of betadine and ethanol again after the vagotomy procure.
- d. Large hole in the surgical drape for the limb region- the surgical drape will be cut to fit the limb more snugly and limit contamination even further.
- e. The surgical tools used for each animal will be logged. This may facilitate tracing sources of infection originating from surgical instruments.

The animals involved in this incident are funded by the following grant:

- National Institutes of Health: R01AR071431: *OA Pathogenesis beyond Cartilage: A preclinical study of the sources of OA pain.*

The University of Florida is committed to protecting the welfare of animals used in research and appreciates the guidance and assistance provided by OLAW in this regard. Should you have any questions regarding this report, please contact Daniel R. Brown, Ph.D., IACUC Chair.

Thank you for your consideration of this matter.

Sincerely,

(b) (6)

David Norton, Ph.D.
Vice President for Research
Institutional Official

(b) (6)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, June 9, 2021 7:38 AM
To: Research - IACUC
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Reportable adverse event (2021Apr02) [ref:_00D412ElGo_5001K11l6Y:ref]

Thank you for this report. We will send a response soon.
Axel Wolff

From: Research - IACUC <iacuc-crm@research.ufl.edu>
Sent: Tuesday, June 8, 2021 12:41 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: drbrown@ufl.edu; (b) (6)
Subject: Reportable adverse event (2021Apr02) [ref:_00D412ElGo_5001K11l6Y:ref]

To All Concerned,

Please see the attached report of an adverse event from the University of Florida (D16-00244). A preliminary report was not sent regarding this adverse event.

The protocol involved in this adverse event is funded by the NIH and the applicable program official and grants management specialist are cc'd on this email.

Please acknowledge receipt and let me know if you have any questions.

Best,

(b) (6)

