



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 1, 2022

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

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 January 26, 2022 letter. The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your May 20, 2022 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Florida, following up on an initial report on May 4, 2022. According to the information provided, OLAW understands that eight rats died or required euthanasia due to a dosing error on the part of the laboratory staff in preparing a nonsteroidal anti-inflammatory drug. Specifically, the concentration was five times higher than the approved dose.

The corrective actions consisted of counseling the laboratory staff on being more attentive when preparing agents for animal dosing, using a locked document which does not allow doses to be changed from the approved calculation, having two laboratory staffers verify calculations, and reviewing dosages during laboratory surgical planning sessions.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the institution to comply with the PHS Policy.

Sincerely,

(b) (6)

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

cc: IACUC Chair



Office of the Vice President for Research

(b) (4) Grinter Hall
PO Box 115500
Gainesville, FL 32611-5500
(b) (6)

May 20, 2022

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 a noncompliance regarding a dosing error which led to rat death / euthanasia. A preliminary report was sent by IACUC Chair Dr. Daniel R. Brown on May 4, 2022.

During preparation for the study, study staff mistakenly thought the meloxicam being used had a concentration of 1 mg/mL. The concentration of meloxicam being used was actually 5 mg/mL; thus when the doses were drawn and the drug was administered, the animals received 5 times more than the approved dose of meloxicam. Due to both the dosing mistake and the advanced age of the animals (Fisher rats acquired from the NIA rodent colony), 8 animals died or were euthanized as part of a humane endpoint.

The IACUC full committee voted on May 17, 2022 that this incident was a noncompliance. The following corrective actions were implemented by the lab:

The incident was discussed with the veterinary staff and then reviewed at a lab meeting with the entire staff. The entire team was made aware of the mistake to insure that more vigilance would be taken in the future. In addition, the lab has made the following changes to standard operating procedures:

1. For schedule C drugs like buprenorphine, the lab's dosing calculations were conducted in a locked excel document, such that only certain fields could be altered. In this type of document, the animal dose cannot be changed without the spreadsheet password, thereby assuring that the doses align with the IACUC protocol. Moving forward, they will update the prescription drug dosing sheets to be password protected in a similar fashion to the schedule C drugs, such that only the lab's IACUC study coordinator and the PI will be able to alter the dose fields.

2. Meloxicam dosing sheet calculations were also being handled by the same individuals injecting the drugs with no secondary verification. However, for schedule C drugs like buprenorphine, doses are checked by a second person when the drug was checked out, allowing mistakes to be caught before administering the drug to the animal. Moving forward, doses of prescription drugs will be verified by two staff members before administration of the drug. This will include the person administering the drug and a more senior staff member (i.e. either the lab's IACUC study coordinator or the PI).
3. The lab already has planning sessions for each surgery and endpoint, which are conducted in a laboratory meeting the week before the surgery or endpoint date. Review of drug doses will be immediately added to these planning meetings.

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

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Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, June 1, 2022 7:21 AM
To: Research - IACUC
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: [EXTERNAL] University of Florida-Reportable noncompliance (2022May01) [ref:_00D412ElGo._5001K18pYx1:ref]

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

Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: Research - IACUC <iacuc-crm@research.ufl.edu>
Sent: Wednesday, May 25, 2022 4:05 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: drbrown@ufl.edu; (b) (6) Kirilusha, Anthony (NIH/NIAMS) [E] <anthony.kirilusha@nih.gov>; Do, Teresa (NIH/NIAMS) [E] <dote@ep.niams.nih.gov>
Subject: [EXTERNAL] University of Florida-Reportable noncompliance (2022May01) [ref:_00D412ElGo._5001K18pYx1:ref]

To All Concerned,

I am sending the attached report of a noncompliance from the University of Florida (D16-00244). IACUC Chair Dr. Daniel R. Brown sent a preliminary report on May 4, 2022.

The protocol involved in this noncompliance 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,

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Wolff, Axel (NIH/OD) [E]

A3377-82

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, May 6, 2022 7:38 AM
To: Brown, Daniel R
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Potential IACUC Non-compliance

Thank you for this preliminary report, Dr. Brown. We will open a new case file and look forward to receiving the final report from the IO after the IACUC has completed its investigation.

Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: Brown, Daniel R <drbrown@ufl.edu>
Sent: Wednesday, May 4, 2022 11:29 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: [REDACTED] (b) (6)
Subject: [EXTERNAL] Potential IACUC Non-compliance
Importance: High

To All Concerned,

This is preliminary report of a situation potentially involving failure to adhere to an IACUC-approved protocol at the University of Florida (Assurance #D16-00244). Briefly, on 4/29/2022 it was self-reported to the IACUC that 8 rats died or were euthanized after accidental overdose of meloxicam. The approved osteoarthritis study involved (UF protocol #201908739) is funded by NIH.

After consultation with a UF Animal Care Services veterinarian, the following three corrective actions are proposed:

- 1) The PI will update the drug dosing sheets to be password protected, such that only the lab's IACUC study coordinator and the PI will be able to alter the dose fields.
- 2) Doses of prescription drugs will be verified by two study staff members before administration of each drug. This will include the person administering the drug and a senior staff member (IACUC study coordinator or the PI).
- 3) Drug doses will be reviewed during the planning sessions for each surgery and end point, which are conducted in laboratory meetings each week before the surgery or end point date.

The situation will be reviewed by the UF IACUC at its next convened meeting. A final report is expected within 30 days.

Please contact me with any questions or concerns.

Dan Brown



Daniel R. Brown, PhD
Chairman, UF Institutional Animal Care and Use Committee
Associate Professor of Infectious Diseases & Immunology
College of Veterinary Medicine
University of Florida
Gainesville FL 32611-0880 USA

(b) (6)

drbrown@ufl.edu

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