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

October 15, 2021

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

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 September 27, 2021 letter reporting an adverse event at the University of Florida (UF) following up on an initial August 18, 2021 notification by email.

According to the information provided, this Office understands that the UF Animal Care and Use Committee (ACUC) determined that an adverse event occurred with respect to: unanticipated development of blistered feet in rats on a protocol approved study. The final report states on July 1, 2021, thirteen rats developed large fluid filled blisters on their hind feet after administration of paynantheine and speciogynine followed by a hot plate time course assay as described in the IACUC-approved protocol. Ultimately, the animals were humanely euthanized following consultation with the Animal Care Services (ACS) veterinarian.

It was concluded the single bolus doses in combination with exposure to the hot plate assay was likely the root cause of the incident. The IACUC voted the incident was reportable on September 21, 2021 and the following corrective actions were implemented:

- The laboratory will no longer use the hot plate assay.
- A modification to the protocol will be submitted within 2 weeks to remove the assay from all protocols.

It is noted that this research project is supported by PHS funding and the NIH funding component has been notified of the event. Based on its assessment of this explanation, OLAW understands that the University of Florida has implemented appropriate measures to correct and prevent recurrence of this type of event.

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: 2021.10.15 09:00:05 -04'00'

Jacquelyn Tubbs, DVM, DACLAM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact

UF | UNIVERSITY of FLORIDA

Office of the Vice President for Research

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

September 27, 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 and PHS Policy IV.F.3., provides this report of an adverse event regarding rats that developed blistered feet following a hot plate assay. This is a follow up to a preliminary report sent to OLAW on August 18, 2021 by IACUC Chair Dr. Daniel R. Brown.

On July 1, 2021, 13 rats developed large fluid filled blisters on their hind feet after administration of paynantheine and speciogynine followed by a hot plate time course assay as outlined in the approved IACUC protocol. All affected rats were euthanized after consultation with an Animal Care Services (ACS) veterinarian.

An assessment was completed by the laboratory in collaboration with the ACS vet to identify the cause of the adverse event. It was determined that the single bolus drug doses in combination with exposure to the hot plate likely caused the adverse event. It may be that there was an interaction between drug effects and assay parameters, but this was not confirmed.

The IACUC full committee voted on September 21, 2021 that this incident was an adverse event and was reportable through the IO to regulatory agencies. The following corrective actions have been implemented:

1. The laboratory will no longer use the hot plate assay.
2. A modification to the protocol will be submitted within 2 weeks to remove this assay from all protocols.

This study is funded by the following grant:

- National Institutes of Health: UH3DA048353 *Opioid use disorders: UF Pharmacy medications discovery and development.*

The NIH funding components have been notified of the adverse event.

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:** Friday, October 1, 2021 7:44 AM
**To:** Research - IACUC
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)
**Subject:** RE: University of Florida-Reportable adverse event-2021Aug01 [ ref:_00D412ElGo._5001K13j0Oa: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:** Thursday, September 30, 2021 11:47 AM
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
**Cc:** drbrown@ufl.edu; (b) (6) Acri, Jane (NIH/NIDA) [E] <jacri@nida.nih.gov>
**Subject:** University of Florida-Reportable adverse event-2021Aug01 [ ref:_00D412ElGo._5001K13j0Oa:ref ]

To All Concerned,

Please see the attached report of an adverse event from the University of Florida (D16-00244). This is a follow up to a report sent by Dr. Daniel R. Brown on August 18, 2021.

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

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

(b) (6)

---------- Forwarded Message ----------
**From:** (b) (6)
**Sent:** 9/28/2021, 8:41 AM
**To:** iacuc-crm@research.ufl.edu; operations@research.ufl.edu
**Cc:** (b) (6)
**Subject:** RE: For IO signature-University of Florida-Reportable adverse event-2021Aug01 [ ref:_00D412ElGo._5001K13j0Oa:ref ]

(b) (6)

Attached is the signed copy of the reportable adverse event-2021Aug01 document.

*Kindest regards,*

(b) (6)

**From:** Research - IACUC <iacuc-crm@research.ufl.edu>
**Sent:** Monday, September 27, 2021 1:57 PM
**To:** RES-Operations <operations@research.ufl.edu>
**Cc:** Brown,Daniel R <drbrown@ufl.edu>
**Subject:** For IO signature-University of Florida-Reportable adverse event-2021Aug01 [ ref:_00D412ElGo._5001K13j0Oa:ref ]

[External Email]

A3377 -8P

**Wolff, Axel (NIH/OD) [E]**

**From:** OLAW Division of Compliance Oversight (NIH/OD)
**Sent:** Wednesday, August 18, 2021 11:22 AM
**To:** Brown,Daniel R
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)
**Subject:** RE: Potential IACUC Adverse Event

Thank you for this preliminary report, Dr. Brown. We will start a new case file.

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

**From:** Brown,Daniel R <drbrown@ufl.edu>
**Sent:** Wednesday, August 18, 2021 9:58 AM
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
**Cc:** (b) (6)
**Subject:** Potential IACUC Adverse Event
**Importance:** High

To All Concerned,

This is preliminary report of a situation involving animal injury due to behavioral testing at the University of Florida (Assurance #D16-00244). Briefly, it was self-reported to the IACUC that 13 rats developed blistered feet within 24 hr after a hotplate response latency test used to assess the sedative effects of drugs according to an IACUC-approved protocol. The rats were euthanized after immediate veterinary consult. Upon initial IACUC investigation the likely cause was the dose of drugs being tested in the assay.

The incident was discussed at our IACUC Full Committee meeting on 8/17/21 and necessary corrective actions will be finalized within 2 weeks. A final report will be discussed at the next convened IACUC meeting and a final report will be sent to OLAW.

Please contact me with any questions or concerns.

UF UNIVERSITY of FLORIDA

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