



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 28, 2021

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

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 18, 2021 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 27, 2021. According to the information provided, OLAW understands that 60 mice were found moribund or dead after receiving an irradiation dose that was too high. A new irradiator had been installed and the research staff failed to use the appropriate filter which contributed to the overdose. Although the laboratory member had been trained with Radiation Safety, the new machine requires extra steps and different restrained chambers.

The corrective actions consisted of euthanizing the surviving mice, having laboratory receive retraining by Radiation Safety, and obtaining the correct restraint chambers. The new machine cannot be used until staff has been trained using live animals and assessed for competency.

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. It is only necessary to send a follow up report if the corrective actions are not completed as proposed or additional problems develop with the animals or machine. 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



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 18, 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 a noncompliance regarding mice that received improper irradiation dose causing death. A preliminary report was sent via email on May 27, 2021 by IACUC Chair Dr. Daniel R. Brown. .

On May 3, 2021, Animal Care Services (ACS) found thirteen cages of moribund or dead mice (60 mice). These mice received a tumor intracranial injection on April 19, 2021 and 5 Gy irradiation on April 25, 2021. A new irradiator had been placed in the Biomedical Sciences Building in March, this was the first set of animals the laboratory had irradiated with the new machine. After this incident the laboratory met with UF Environmental Health & Safety (EH&S) Radiation Control Officer and it was admitted by lab staff that the appropriate irradiator filter had not been used with this group of mice. As a result, the animals were likely overdosed. It was concluded that their severe acute decline or death was caused by the overdose, because this had not been witnessed by the lab in the past. The surviving animals were euthanized by the lab for tissue collection. Splenic atrophy was noted in each mouse, likely caused by the irradiation overdose.

The lab member who performed the irradiation had received training with Radiation Safety on the general use of the new machine and had been allowed restricted access before performing irradiation. The new irradiator requires many additional steps that the previous machine did not, likely contributing to user error in this incident. The new training material was reviewed during the initial IACUC investigation. It was noted that the manual provided to the laboratories was difficult to follow. No additional live animal training is currently being provided.

Additional concerns regarding use of improper irradiation accessories were noted. Restraint chambers designed for the old unit had been used. This may have contributed to improper radiation doses.

Report of a noncompliance
June 18, 2021
Page 2

The IACUC full committee voted on June 8, 2021 that this incident was a noncompliance. The following corrective items have been implemented:

1. Lab staff involved in this incident have been re-trained by EH&S Radiation Safety.
2. The rodent restraint accessories made specifically for this irradiator have been obtained for common use. Use of restraints from the old machine has been prohibited.
3. Access to the new irradiator has been prohibited for all users until UF personnel have been designated to provide live-animal irradiator training and serve as the point of contact for oversight of this unit. UF EH&S will continue to provide general training on radiation, however additional hands-on training for all users of the new irradiator and animal irradiation oversight expertise in particular will be required before animal experiments can continue. Once these items are completed a follow up report will be sent to OLAW.

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

- Department of Defense-USAMRAA-W81XWH2010726-*Clinical Development of CAR T Cell Therapy Targeting CD70 in Primary Glioblastoma*

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

mpm gw

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, May 28, 2021 7:16 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.
Axel Wolff

From: Brown, Daniel R <drbrown@ufl.edu>
Sent: Thursday, May 27, 2021 9:21 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: [REDACTED] (b) (6)
Subject: Potential IACUC Non-Compliance
Importance: High

To All Concerned,

This is preliminary report of a situation involving animal death due to improper irradiation at the University of Florida (Assurance #D16-00244). Briefly, it was self-reported to the IACUC that 60 mice died unexpectedly soon after irradiation. Upon initial investigation the likely causes identified are (1) use of irradiation chambers from an older model of irradiator that do not exactly match this newer instrument, and (2) ineffective training on how to use the new irradiator.

Access to this irradiator has been temporarily prohibited for all users, and IACUC staff and I have initiated a full investigation. A final report to our IACUC 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
Tel [REDACTED] (b) (6)
Fax [REDACTED]
drbrown@ufl.edu