



DEPARTMENT OF HEALTH & HUMAN SERVICES

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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

July 9, 2021

Re: Animal Welfare Assurance
#A3272-01 (OLAW Case 2J)

Dr. Denis Wirtz
Vice Provost for Research
Johns Hopkins University
3400 N. Charles Street
Baltimore, MD 21218

Dear Dr. Wirtz,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your July 1, 2021 regarding an allegation of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Johns Hopkins University (JHU). The allegation was referred to OLAW by another NIH oversight office for investigation of the animal issues and we requested assistance from the JHU Institutional Animal Care and Use Committee (IACUC) chair to determine the facts. According to the information provided, OLAW understands that 34 out of 165 mice on an approved stroke study exhibited redness or necrosis of the tail following surgery. The veterinary staff was contacted to provide care to the mice and to further examine the root cause. It was discovered that a new infrared heating pad was being used to warm the mice following the stroke procedure and that this produced the tail lesions.

The corrective actions consisted of modifying the protocol to use only heating pads that do not emit infrared radiation, to not secure the tails to the pad, and to use an insulating layer between the heating device and animal to prevent overheating of the tail. The implementation of these procedures has resulted in no further adverse clinical outcomes.

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 IACUC to comply with the PHS Policy and we will inform the other NIH oversight office accordingly. Thank you for your prompt attention to this matter.

Sincerely,

(b) (6)

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

cc: IACUC contact
Kerry Gastley, NINDS Grants Management Specialist



July 1, 2021

Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare
National Institutes of Health
Bethesda, Maryland 20892-6910

RE: Response to OLAW Referral of an Animal Welfare Concern --D16-00173 (A3272-01)

Dear Dr. Wolff:

Please accept this letter as a response to the matter you referred to the then Chair of the Johns Hopkins University Animal Care and Use Committee, Dr. Nancy Ator, on March 2, 2021. You relayed that OLAW had received an anonymous report that unexpected post-operative outcomes were occurring in mice in a research project focused on improving treatment of patients who suffer ischemic stroke. The goal of the research is to identify neuroprotective agents that can be used in stroke patients who must undergo thrombectomy (removal of a blood clot from a blood vessel). The project is supported by the Stroke Preclinical Assessment Network (SPAN), 5U01-NS-113444-02. In accordance with our procedures, this matter was investigated by the ACUC to understand the problem and to determine whether there were any animal welfare or compliance concerns that needed to be considered by the ACUC.

The required surgical procedure of middle cerebral artery occlusion followed by behavioral testing has been used productively and humanely for many years in support of this research. In several recent experiments a minority of the mice studied (34 out of 165) developed redness or necrosis on the tail three to seven days after surgery that could progress to loss of part of the tail. Given this unanticipated outcome for the animals, our clinical veterinarian specializing in work with rodents was promptly contacted by the Principal Investigator. The veterinarian and veterinary staff provided appropriate and prompt care to the animals actively impacted and worked with the lab to assess the possible cause(s). Initial thinking was that the problem might have to do with putting pressure on the tail to prompt the mouse to move in a sensorimotor analysis test. Thus, the procedure was changed to softly touch the tail with a cotton-tip applicator for this purpose. But the problem persisted in some mice.

The clinical veterinarian and the study team next analyzed all aspects of the surgical procedures, including equipment used to warm the animals, procedures used to secure the anesthetized animal, the duration of the surgical procedure, and whether a stroke was produced. No one of these variables alone was found to be responsible. Ultimately it was concluded that the tail inflammation only occurred when a stroke was induced and the mouse was on a newly acquired infrared heating pad for 90 minutes. It was determined that the procedures should be modified to ensure that the stroke surgery included the following: (1) use of a heating pad that does not emit infrared radiation, (2) no securing of the tail to the heating pad, and (3) use of a black pad between the tail and the heating pad to prevent over-heating of the tail regardless of the duration of the surgery. With these changes in procedure, no mouse has since exhibited the problem.

Office of the Provost

265 Garland Hall 3400 N. Charles Street Baltimore, MD 21218 410-516-8070 <http://web.jhu.edu/administration/provost>

Obtained by Rise for Animals.
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The Johns Hopkins Animal Care and Use Committee was informed of the successful analysis and resolution of this clinical problem at its meeting on May 20th, including the discoveries related to the infrared heating pad. The Committee deemed no further corrective actions were necessary and considers this matter closed. Please let us know if you require further information.

Sincerely,

(b) (6)

Denis Wirtz, Ph.D.
Vice Provost for Research

cc: AAALAC International
Brendan J. Canning, Ph.D., Chair, Johns Hopkins University Animal Care and Use Committee
Eric Hutchinson, D.V.M., DACLAM, Attending Veterinarian and Assistant Vice Provost for
Animal Research and Resources, Johns Hopkins University

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, July 2, 2021 7:21 AM
To: Nancy Ator
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Johns Hopkins University Final Report--PDF version

Thank you for this final report, Dr. Ator. I will carefully review and send a response to the IO soon.
Axel Wolff

-----Original Message-----

From: Nancy Ator <ator@jhmi.edu>
Sent: Thursday, July 1, 2021 11:04 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: AAALAC International <accredit@AAALAC.org>; Denis Wirtz <wirtz@jhu.edu>; Brendan Canning <bjc@jhmi.edu>; Eric Hutchinson <ehutchi8@jhmi.edu>
Subject: Johns Hopkins University Final Report--PDF version

Attached please find the pdf of our final report regarding an animal welfare concern that Dr. Wolff referred to me in March of this year.
Please disregard the WORD version sent a short time ago.

Best regards,

Nancy A. Ator, Ph.D.
Immediate Past Chair
Johns Hopkins University Animal Care and Use Committee

Nancy A. Ator, Ph.D.
Professor Emerita
Department of Psychiatry and Behavioral Sciences Division of Behavioral Biology Johns Hopkins School of Medicine
ator@jhmi.edu