DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Laboratory Animal Welfare
6700B Rockledge Drive, Suite 2500 – MSC 6910
Bethesda, Maryland 20892-7982
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) 402-7065

DATE: October 17, 2018

TO: Michael M. Gottesman, M.D.
Deputy Director for Intramural Research, NIH

FROM: Director
Division of Compliance Oversight, OLAW

SUBJECT: Animal Welfare Investigation (#013-18) - Animal Welfare Assurance A4149-01 [Case 12M]

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your October 2, 2018 memo regarding an incident of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the National Institute on Drug Abuse (NIDA). According to the information provided, OLAW understands that on August 25, 2018 a group of four transgenic mice was discovered with footpad swelling, blackened hard digits, and/or skin lesions. One mouse was immediately euthanized and the others were placed under veterinary care until September 4, 2018 when they were euthanized in consultation with laboratory staff. The mice had been subjected to formalin injection which was approved on a separate protocol to be injected into wild-type mice only. In addition, mice were to be euthanized 90 minutes after injection of the formalin. Also, the transgenic mice had previously received surgery, which should not have been followed by formalin injection.

Corrective and preventive actions included stopping all formalin injections, counseling of the PI and lab personnel regarding protocol compliance, refining endpoints and reducing and refining animal numbers. The PI and laboratory personnel were also required to re-take applicable NIH training courses and to attend a presentation on protocol non-compliance reporting requirements.

The actions taken to resolve the issues and prevent recurrence were appropriate and accepted by OLAW. We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

(b) (6)

Brent C. Morse, DVM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: Dr. Stephen Denny
Dr. Richard Wyatt, OAI/OD
Alexander F. Hoffman, Ph.D., Chair, NIDA ACUC

A4149-12M

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

www.nih.gov

October 2, 2018

TO: Brent C. Morse, D.V.M.
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare

FROM: Deputy Director for Intramural Research, NIH

SUBJECT: Animal Welfare Investigations - Assurance A4149-01 (#013-18)

This correspondence conveys the results of an investigation by the National Institute on Drug Abuse, in accordance with Assurance A4149-01 and PHS Policy IV.F.3. The adverse event involved a failure to follow a NIDA ACUC-approved animal study protocol.

The event was first reported to the NIH Office of Animal Care and Use by the NIDA Attending Veterinarian on August 28, 2018. The details of the ACUC investigation and the corrective actions taken by the animal care program are outlined in the attached memorandum.

Please contact me or Dr. Stephen Denny, Acting Director, Office of Animal Care and Use, if additional information or clarifications are required.

(b) (6)

Michael M. Gottesman, M.D.

Attachment

cc: Dr. Wyatt
Dr. Hoffman
Dr. Denny

National Institute
on Drug Abuse
Intramural Research Program

National Institutes of Health
National Institute on Drug Abuse
251 Bayview Boulevard
Suite 200
Baltimore, MD 21224

TO: Dr. Michael Gottesman, Deputy Director for Intramural Research
FROM: Alexander F. Hoffman, Chair, NIDA Animal Care and Use Committee
DATE: October 1, 2018
SUBJECT: Reportable incident on protocol non-compliance

The National Institute on Drug Abuse Intramural Research Program, in accordance with Assurance A4149-01 and PHS Policy IV.F.3., reports the following incident of protocol non-compliance involving the use of hindpaw formalin injections in mice under a protocol entitled "Viral-mediated investigations of neuronal circuits of pain modulation and opiate reward in mice." A summary of the incident, major findings, and proposed remedies are described below.

Summary of incident: On 8/25/2018, a group of 4 transgenic mice was discovered by veterinary/animal care staff as having footpad swelling, blackened hard digits, and/or skin lesions. One of the mice was immediately euthanized by the facility clinical veterinarian, who notified the ACUC Chair and Animal Program Director. The remaining animals were immediately placed under veterinary care and monitored over the next several days. The remaining 3 mice were euthanized in consultation with laboratory staff on 9/4/2018. The mice were listed on ASP #15-INRB-2, and the cage card indicated that mice had received formalin injections. However, this protocol was not approved by the ACUC for formalin injections. Upon speaking with the PI and laboratory staff, it was determined that the animals in fact should have been assigned to a different protocol within the laboratory (ASP #16-INB-4), that does provide for formalin injections. However, ASP #16-INB-4 stipulates that animals are to be euthanized 90 minutes following formalin injection. In addition, the formalin injections approved under #16-INB-4 were approved only in wildtype mice, not in the transgenic line. Further, these transgenic mice had previously received surgery. Although the surgery had been approved on ASP #16-INB-4, the protocol did not stipulate that the same surgical animals would also be receiving formalin injections.

Findings:

The PI failed to adhere to the following protocol requirements:

(1) Maintaining appropriate tracking of animals (e.g., moving from one protocol to another)
(2) Following the procedures as described in the ASP

(3) Providing appropriate post-treatment care or alleviation of pain/distress as indicated in the ASP in the alternative endpoints and the 90 minute experimental endpoint.

Based on these findings, it is clear that this incident represents a violation of animal welfare standards, and constitutes a reportable animal welfare incident under OLAW Guidelines.

After meeting with both the ACUC Chair and Animal Program Director, the following corrective actions were taken. First, the PI and lab personnel agreed to immediately suspend all formalin injections. Second, the PI and lab personnel were provided with a copy of both the most recent version of the approved ASP and the NIH Animal Research Advisory Committee (ARAC) Guidelines "Guidelines for Pain and Distress in Laboratory Animals: Responsibilities, Recognition and Alleviation." Upon receipt of these items, all lab personnel were required to (1) reaffirm that they understood their respective responsibilities on the study, and (2) affirm that they had read and understood the ARAC guidelines. Third, the PI agreed that in order to perform any future experiments involving formalin injections, a modification to the proposal must be submitted to the ACUC for approval. Fourth, the Chair and Animal Program Director discussed with the PI the need to (1) incorporate a thorough justification of the proposed experimental design; (2) provide clear documentation of the recognition of alternative endpoints; and (3) minimize/refine animal numbers to the greatest extent possible, consistent with the experimental objectives. Finally, the PI agreed to properly document transfer of animals between protocols within the lab.

These actions were reviewed and approved by the ACUC during its meeting on September 27. The ACUC also voted to require the PI and laboratory personnel to re-take the NIH Training Courses for PI's and Animal Users, respectively. In addition, the PI and lab personnel were required to attend a NIDA-IRP wide presentation regarding protocol non-compliance reporting requirements.

The ACUC believes that the frank discussions with the PI and lab personnel, coupled with the requirements and assurances documented above, will reduce the likelihood of further re-occurrences of this type of incident. In addition, the post-approval verification (PAV) program may be used to provide assurance of protocol compliance in this and other protocols. The NIDA IRP ACUC is committed to the highest animal welfare standards, and appreciates the support of OLAW in this regard. Should you have any additional questions or concerns regarding this report, please do not hesitate to contact me.

Sincerely,

(b) (6)

Alex Hoffman, Ph.D.
Chair
NIDA IRP Animal Care and Use Committee

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, October 09, 2018 1:46 PM
To: Denny, Stephen (NIH/OD) [E]; OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: A4149-01 NIH Animal Incident Report (NIDA #013-18)

Thank you for this final report Dr. Denny We will send an official response soon. Please consider submitting prompt preliminary reports as was OACU's previous practice. If you have any questions, please feel free to contact me.

Best regards, Brent Morse

Brent C. Morse, DVM, DACLAM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: Denny, Stephen (NIH/OD) [E]
Sent: Tuesday, October 09, 2018 11:18 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: A4149-01 NIH Animal Incident Report (NIDA #013-18)

Dear OLAW/DCO,

Final reports from the NIH Institutional Official and the National Institute on Drug Abuse ACUC addressing an animal incident reported to this office on 5 September are attached. The incident involved a principal investigator failing to use research naïve mice in his ACUC-approved study and failing to implement an ACUC-approved study endpoint at the appropriate time.

If you have any questions please contact me via email or the phone number listed below. Thanks, Steve

STEPHEN L DENNY, DVM, MS, DACLAM | Acting Director, Office of Animal Care and Use | National Institutes of Health | Bldg 31-Rm B1C37, 9000 Rockville Pike, Bethesda, MD 20982 | Phone: (301) 496-5424 | http://oacu.od.nih.gov