



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE  
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:  
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Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

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April 2, 2018

Re: Animal Welfare Assurance  
#A3294-01 (OLAW Case 2G)  
IACUC Case # 2018 - 02

Dr. Jennifer Larsen  
Vice Chancellor for Research  
Louise and Morton Degen Professor of Internal Medicine  
University of Nebraska Medical Center  
987878 University Nebraska Medical Center  
Omaha, NE 68198-7878

Dear Dr. Larsen,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 27, 2018 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the University of Nebraska Medical Center. According to the information provided, OLAW understands that two researchers attempted to unsuccessfully collect cerebrospinal fluid (CSF) from the cisterna magna of an anesthetized nonhuman primate and that following recovery, the primate exhibited neurological signs.

The initial action taken following the unsuccessful tap consisted of a veterinarian collecting the CSF from the lumbar region. After showing the adverse clinical signs, the animal was euthanized and necropsied. The pathology report indicted hemorrhage in the brainstem. The research staff indicated that in order to obtain a CSF sample, multiple attempts are often performed by two individuals. The corrective action consisted of Comparative Medicine Research Technical Services overseeing all subsequent animal activities on this protocol. The Institutional Official directed the Institutional Animal Care and Use Committee to evaluate the policies and procedures for evaluating the training and experience of staff performing invasive procedures and/or working with nonhuman primates. Also, Comparative Medicine is to create a dedicated care team to reduce the number of individuals involved with animal activities using nonhuman primates. All CSF collection protocols in primates were updated to include potential complications due to this procedure.

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

March 27, 2018

Axel V. Wolff, M.S., D.V.M., Director  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
Rockledge 1, Suite 360, MSC 7982  
6705 Rockledge Drive  
Bethesda, MD 20892-7982

**RE: IACUC Case #2018-02**

Dear Dr. Wolff:

I am submitting this report in accordance with the requirements of the PHS Policy at IV.F.3. The IACUC has reviewed this adverse event described in this report and categorized it as serious and, therefore, reportable to OLAW.

1. **Animal Welfare Assurance Number:** A3294-01
2. **Grant or Contract Number:** NIH 5R01AI113883-04 NIH/NIMH 1R21MH113455-01
3. **Species:** Nonhuman primates
4. **Effects on Programmatic or Physical Areas:** NA
5. **Explanation of the Situation:**
  - a. Research staff anesthetized an NHP at approximately 10:30 AM to perform a rectal biopsy, blood collection, and cerebral spinal fluid collection. Two research personnel alternated attempts to collect Cerebral Spinal Fluid (CSF) from the cisterna magna, but neither were successful. Both personnel maintain records confirming completion of training for the CSF collection procedure.
  - b. A Comparative Medicine (CM) veterinarian was contacted to provide assistance. The veterinarian successfully collected the CSF sample from the lumbar region.
  - c. The animal health record noted that the animal was alert and active at 12:00 PM, but at 3:45 PM CM husbandry staff notified a CM veterinarian that the NHP was displaying abnormal behavior. The CM veterinary observations included nystagmus (rapid involuntary movements of the eyes), anisocoria (uneven pupil size), head pressing and head tilt. After evaluation and consultation by CM veterinarians it was determined that the animal should be euthanized. A necropsy and tissue collection were performed by the CM veterinarians.
  - d. The pathology report summary: "the neurologic deficits were likely due to hemorrhage in the brainstem. Hemorrhage in the brainstem is often accompanied by localized swelling and increased intracranial pressure, which if present, may have contributed to the neurologic deficits noted on clinical exam."
  - e. The Attending Veterinarian (AV), CM clinical veterinarians, an IACUC Chair and the Protocol Assessment Liaison (PAL) met with the Principal Investigator (PI)

and the research staff. Research staff explained that there are times when additional attempts are required in order to successfully obtain a CSF sample. They also included that there are usually two trained research staff present to assist one another, and if one is unsuccessful they may alternate attempts which was the case this time.

- f. The IACUC Chair and the AV requested immediate oversight by CM Research Technical Services during all procedures to be performed on the NHPs for this protocol and the PI agreed that this would be the best plan moving forward. Research staff were instructed to coordinate schedules with a CM clinical veterinarian.
- g. Per the Institutional Official (IO) the following action has been requested in response to a previously reported incident, but covers all nonhuman primate research at UNMC and is relevant to this incident.
  - 1) "The IACUC will re-evaluate its current policy and process for confirming past experience and/or training of staff performing invasive procedures and/or working with nonhuman primates." In Progress
  - 2) "Requested the comparative medicine program create a dedicated care team to reduce the number of personnel involved with care and research involving nonhuman primates. This dedicated care team will coordinate and provide oversight of procedures involving nonhuman primates until review of the above is complete and final recommendations are made."  
In Progress
- h. PAL requested the following update to NHP protocols approved for CSF collection:
  - 1) Please include in the change summary: **This is an update to potential complications associated with CSF collection as indicated in the June 2017 Association of Primate Veterinarians' Position Statement: Cerebrospinal Fluid Aspiration for Nonhuman Primates in Biomedical Research** Complete
  - 2) Please revise Section VIII. 2. C. Please include the following sentence for potential health consequences for **CSF Collection**:  
**"Known complications could include hemorrhage, herniation, infection, spinal cord or nerve root damage and animal discomfort."**  
Complete

#### 6. Actions Taken by the IACUC:

- a. Following review of this incident by the IACUC subcommittee (IS) they voted (7 in favor, 0 against, 0 abstentions) that this incident was an adverse event that impacted animal welfare and should therefore be reported. The subcommittee also determined that the corrective/preventative action plan was sufficient.
- b. On 3/29/18 the IO accepted all recommendations of the IS as written.

**7. Implementation Schedule:**

- a. All corrective/preventative action has been initiated and noted as complete or in progress.

If you have any questions or require any further information, please do not hesitate to contact me.

Respectfully,

(b) (6)

Jennifer Larsen, MD  
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University of Nebraska Medical Center  
Vice Chancellor for Research  
Louise and Morton Degen Professor of Internal Medicine  
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cc: Robert G. Bennett, Ph.D., IACUC Executive Chair

(b) (6)

John F. Bradfield, D.V.M., Ph.D. Attending Veterinarian/Director Comparative  
Medicine

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

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Friday, March 30, 2018 12:41 PM  
**To:** (b) (6)  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: Initial Report of Adverse Event UNMC/UNO IACUC Case #2018-02

Thank you for this report, (b) (6) We will send a response soon.  
Axel Wolff

**From:** (b) (6) @unmc.edu]  
**Sent:** Friday, March 30, 2018 12:10 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** Larsen, Jennifer L <jlarsen@unmc.edu>; Bennett, Robert G <rgbennet@unmc.edu>; (b) (6)  
(b) (6) Bradfield, John F <john.bradfield@unmc.edu>; IACUCORA, UNMC  
<IACUCORA@unmc.edu>  
**Subject:** Initial Report of Adverse Event UNMC/UNO IACUC Case #2018-02

March 30, 2018

Axel V. Wolff, M.S., D.V.M., Director  
Division of Compliance Oversight  
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National Institutes of Health  
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**RE: IACUC Case #2018-02**

(b) (6)

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