



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive - MSC 7982
Bethesda, Maryland 20892-7982
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

March 21, 2017

Re: Animal Welfare Assurance
#A3281-01 [OLAW Case 1X]

Francis L. Macrina, PhD
Vice President for Research
Virginia Commonwealth University
Biotech One, Suite (b) (4)
PO Box 980568
Richmond, VA 23298-0568

Dear Dr. Macrina,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 16, 2017 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Virginia Commonwealth University, following up on an initial telephone report on March 6, 2017. According to the information provided, OLAW understands that nine post-surgical rats failed to receive a second dose of analgesia at the timeframe described in the approved protocol. No adverse clinical signs were exhibited by the rats due to this incident.

The corrective action consisted of the investigator counseling the individual responsible and the laboratory staff on appropriate analgesia dosing. The surgical form will indicate morning and afternoon dosing to ensure drugs are given at the right time. The investigator assured the Institutional Animal Care and Use Committee that staff will adhere to the protocol and provide analgesics at the time specified in the protocol.

Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate, correct, and prevent recurrence of the noncompliance. We appreciate having been informed about this matter and find no cause for further action by this Office.

Sincerely,

(b) (6)

Axel Wolff, M.S., D.V.M.
Director
Division of Compliance Oversight

cc: IACUC Chair

(b) (6)



VCU

Office of Research and Innovation

BioTech One, 3rd Floor, Suite 3000
800 East Leigh Street
P.O. Box 980568
Richmond, Virginia 23298-0568

804 827-2262 • Fax: 804 828-2051
TDD: 1-800-828-1120
macrina@vcu.edu

Francis L. Macrina, PhD
Edward Myers Professor of Dentistry and
Vice President for Research and Innovation

March 16, 2017

Axel V. Wolff, M.S., D.V.M., Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
RKL1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982
(301) 594-2061

VCU Animal Welfare Assurance number A3281-01

Dear Dr. Wolff:

Virginia Commonwealth University, in accordance with Assurance A3281-01 and PHS Policy IV.F.3., provides this report of noncompliance. Research staff failed to adhere to the approved IACUC protocol (which calls for providing a 2nd dose of post-op ketoprofen following ICSS (Intracranial Self-Stimulation) following cannula implant in 24 hour intervals) on 9 rats. This incident was reported to you on March 6, 2017 via a telephone call by (b) (6) Office of Research Subjects Protection (ORSP).

Description of Incident

It was noted during a laboratory post approval compliance monitoring visit that 9 rats were administered their 2nd dose of post-op ketoprofen following ICSS cannula implant outside of the 24 hours +/- 1 hour window between the 1st and 2nd dos. The time ranged from 25 hours 15 minutes to 32 hours 7 minutes after the first dose. Only 2 doses are required following this procedure. The investigator has acknowledged this mistake made by his research staff. None of the rats showed notable aberrant behaviors indicative of pain or distress on the 2nd day. The most objective endpoint related to pain and distress is body weight, and these rats did not display unusual body weight changes. Specifically, the mean \pm SEM weights on Day 1 (pre-surgery: (b) (4) grams), Day 2 (day after surgery: (b) (4)), and Day 3 (2 days after surgery: (b) (4)), were not significantly different (one-way ANOVA, $p=0.38$). Additionally, linear regression of individual data indicated no correlation between ketoprofen injection interval and weight change between the 1st and 2nd injection ($p = 0.72$, $R^2 = 0.02$). Lastly, weight changes in this group of rats were similar to weight changes observed in other rats.

Corrective action plan:

The following corrective action plan was implemented:

1. The investigator has already met with lab personnel, including the individual involved in this incident, regarding this issue noted during this PACM visit. Additionally, the investigator reinforced with all staff that follow-up injections of ketoprofen are to be administered 24 \pm 1hr after the initial dose.

2. The investigator has instructed staff to include a.m./p.m. designations on the surgical form to indicate timing of ketoprofen injections as a reminder for the 2nd dose.
3. The investigator assured that 2nd dose will be administered 24 ± 1 hr after the initial dose in future studies involving this protocol.
4. The investigator assured the IACUC that all research staff will carefully review and adhere to the approved IACUC protocol.

After a review of direct costs associated with the procurement, care, drugs and use of animals related to the experiments conducted on the 9 rats, the monetary impact of the noncompliance is considered insignificant and as such it was not necessary to make an adjustment to the grant.

We regret that this incident occurred. Following our detailed investigation, we have deployed specific corrective actions to enhance our program and to minimize future occurrences. The IACUC has discussed this incident at the full committee meeting on February 8th, and will be advised of the above corrective actions at the next full committee meeting.

We appreciate your consideration of VCU's efforts to minimize future occurrences. VCU remains committed to animal welfare and recognizes its ethical responsibilities in ensuring the welfare of research animals and complying with the *PHS Policy* on the Humane Care and Use of Laboratory Animals.

Sincerely,

(b) (6)

Francis L. Macrina, Ph.D.
Institutional Official
Edward Myers Professor of Dentistry and
Vice President for Research and Innovation

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, March 17, 2017 7:59 AM
To: (b) (6)
Subject: RE: Follow-up letters -VCU Assurance# A3281-01 (D16-00180, effective 1/9/2017))

Thank you for these reports, (b) (6) I'll send a response soon.
 Axel Wolff

From: (b) (6)
Sent: Thursday, March 16, 2017 4:20 PM
To: Wolff, Axel (NIH/OD) [E] <WolffA@OD.NIH.GOV>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Francis L Macrina <macrina@vcu.edu>; (b) (6)
Subject: Follow-up letters -VCU Assurance# A3281-01 (D16-00180, effective 1/9/2017))

Dear Dr. Wolff,

Attached please find two follow-up reporting letters signed by Dr. Macrina, VCU Institutional Official. They were reported to you by phone on February 21 and March 6 individually. Each written report includes a detailed explanation of the incident and actions taken by VCU.

We have reviewed these two incidents thoroughly and deployed specific corrective actions designed to enhance our animal program and to prevent future occurrences. We appreciate your consideration and VCU recognizes its responsibilities to comply with the Public Health Service Policy on the Humane Care and Use of Laboratory Animals and the Guide, and also remains committed to animal welfare.

Should you have any questions regarding this matter, please do not hesitate to contact me at (b) (6) or email to: (b) (6)

Best Regards,

(b) (6)

--

(b) (6)

(b) (6)

(b) (6)

Animal Research website: <https://www.vcu.edu/research/acup/index.htm>

Animal Care and Use Program Blog: <http://wp.vcu.edu/acup/>



Initial Report of Noncompliance

By: *aw*

Date: *3/6/17*

Time: *9:10*

Name of Person reporting: *(b) (6)*
Telephone #: *(b) (6)*
Fax #:
Email:

Name of Institution: *VIRGINIA COMMONWEALTH U*
Assurance number: *A3281*

Did incident involve PHS funded activity? *Yes*
Funding component: _____
Was funding component contacted (if necessary): _____

What happened?
9 rats didn't get post op analgesia according to protocol schedule
No problems noted

Species involved: *Rat*
Personnel involved:
Dates and times:
Animal deaths:

Projected plan and schedule for correction/prevention (if known): _____
Will now give drug \pm 1 hr of required time

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY
Case # _____