



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) 402-7065

January 15, 2020

Re: Animal Welfare Assurance
#A3281-01 [OLAW Case 2K]

Dr. P. Srirama Rao
Vice President for Research and Innovation
Virginia Commonwealth University
Biotech One, (b) (4)
PO Box 980568
Richmond, VA 23298-0568

Dear Dr. Rao,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your January 14, 2020 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 December 13, 2019. According to the information provided, OLAW understands that 98 rats that had undergone a corneal graft transplant surgery failed to receive the full dose of analgesic specified in the protocol following the procedure. A lower dose of analgesic was given due to concerns of interference with the study. No signs of pain or distress were noted in the rats and a subject matter expert stated that this procedure has minimal or no pain associated with it because sensory nerves are severed.

The corrective actions consisted of counseling the investigator to always follow the protocol, to consult with a veterinarian regarding concerns with prescribed drugs, and to amend the protocol before implementing changes to the approved drugs. The laboratory staff was counseled to follow the protocol, the protocol was amended to address the analgesic dosing, and any protocol amendments will be discussed with staff.

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
Director for the Animal Care and Use Program



VCU

Office of the Vice President for Research and Innovation

Office of the Vice President for
Research and Innovation
Virginia Commonwealth University

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psrao@vcu.edu

P. Srirama Rao, PhD
Vice President for Research and Innovation

January 14, 2020

Axel V. Wolff, M.S., D.V.M.,
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
6700B Rockledge Drive
Suite 2500, MSC 6910
Bethesda, MD 20892
(301) 496-7163

VCU Animal Welfare Assurance number D16-00180 (A3281-01)

Dear Dr. Wolff,

Virginia Commonwealth University, in accordance with Assurance D16-00180 (A3281-01) and PHS Policy IV.F.3., provides this report of noncompliance regarding failure to adhere to an IACUC-approved protocol. Ms. Chuang, Director of Animal Care and Use Program reported this incident to you on December 10, 2019 via a telephone call.

Description of Incident:

During the post approval compliance monitoring, it was noted that 98 rats had undergone corneal graft transplant surgery and each rat was administered 0.1 ml of Buprenorphine SR Lab (concentration of 1.0 mg/ml) regardless of their body weight rather than the 1.2 mg/kg dose approved in the protocol. The lower dose of Buprenorphine SR lab was given because there was a concern it might have effects with the therapeutic drugs/model. They did not observe any obvious post-operative pain in the rats. The investigator has contacted the Attending Veterinarian to discuss the analgesic plan for rats undergoing corneal procedures. Within their discussion, the investigator's mentor (at another institution) who had considerable experience over 30 years as director of the corneal transplant clinical and research services has confirmed that there is minimal or no discomfort in humans and animals after corneal transplantation. They no longer prescribe their corneal transplant patients analgesics and do not use them in their rat research model. This is because the nerves are actually cut during the procedure and the central portion of the new cornea has no sensation. In summary, systemic or topical opioids are not necessary because there is minimal or no discomfort.

Corrective action plan:

(1) The investigator was counseled that they must follow the approved protocol. If there was concern it may have effects on the therapeutic drugs, they should consult with veterinarians and submit an amendment prior to implementation of any change in analgesic dosing or withdrawal.

(2) The investigator has taken additional measures that this will not happen again, including:

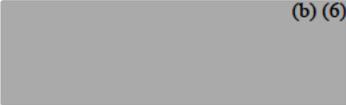
- Counsel all lab members who are involved with animal work to ensure they follow the approved protocol.
- The investigator will go over the protocol changes (based on approved amendments) during their regular weekly meeting, especially the dosing changes of the drugs.
- The investigator has consulted with the attending veterinarian and an amendment regarding the changes in analgesic dosing will be submitted based on the rationale described above provided by the corneal transplant expert.

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 will be advised of the above corrective actions at their 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)



P. Srirama Rao, PhD
Vice President for Research and Innovation

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, January 14, 2020 4:00 PM
To: Kuei-Lan Chuang; Wolff, Axel (NIH/OD) [E]; OLAW Division of Compliance Oversight (NIH/OD)
Cc: Srirama Rao; (b) (6)
Subject: RE: Follow-up letter (VCU Assurance# D16-00180/A3281-01)

Thank you for this report Amy. We'll send you an official response soon.

Best regards, Brent Morse

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

Please note that this message and any of its attachments are intended for the named recipient(s) only and may contain confidential, protected or privileged information that should not be distributed to unauthorized individuals. If you have received this message in error, please contact the sender.

From: Kuei-Lan Chuang [mailto:kchuang@vcu.edu]
Sent: Tuesday, January 14, 2020 12:53 PM
To: Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Srirama Rao <psrao@vcu.edu>; (b) (6)
Subject: Follow-up letter (VCU Assurance# D16-00180/A3281-01)

Dear Dr. Wolff,

Attached please find the follow-up letter signed by Dr. Rao, VCU Institutional Official. I discussed this situation with you earlier and then reported back by phone. The written report includes a detailed explanation of the situation and actions taken by VCU IACUC. In addition, the consultation about the justification has been included based on our phone discussion on 1/10. Thank you!

The ACUP leadership has reviewed this 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: kchuang@vcu.edu.

Best Regards,

--

Amy

Amy Chuang, M.S., RQAP-GLP, CPIA
Director for the Animal Care and Use Program (ACUP)



Box 980568
Richmond, VA 23298

(b) (6)

kchuang@vcu.edu

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

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



Initial Report of Noncompliance

By: *aw*

Date: *12/13/19*

Time: *9:00*

Name of Person reporting: *AMY Cheung*
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?
98 rats had cement transplant but no analgesia given per protocol

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

Projected plan and schedule for correction/prevention (if known): _____
amend protocol

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY
Case # _____