



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE  
NATIONAL INSTITUTES OF HEALTH

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Office of Laboratory Animal Welfare  
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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 3, 2019

Re: Animal Welfare Assurance  
A3157-01 [OLAW Case R]

Mr. David Isaacks  
Medical Center Director  
VA – Harry S. Truman Memorial's Hospital  
800 Hospital Drive  
Columbia, Missouri 65201

Dear Mr. Isaacks,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your December 21, 2018 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Harry S. Truman Memorial Veterans' Hospital, following up on an initial report on November 13, 2018. According to the information provided, OLAW understands that a total of 36 mice were given an unapproved infusion of an experimental hormone at three different timepoints. The laboratory staff was confused as to which protocol the mice were on. The protocol deviation was not reported to the Institutional Official (IO) by the Institutional Animal Care and Use Committee (IACUC) within the required timeframe.

The corrective actions consisted of submitting an amendment to the protocol, which was subsequently approved by the IACUC. The IACUC chair and committee members were counseled on the prompt reporting requirements of noncompliance to the IO. The Principal Investigator (PI) and laboratory manager will discuss the content of the approved protocol with laboratory staff prior to starting animal activities, copies of the protocol will be maintained in the laboratory, animal activities will be reviewed by the PI and staff before starting, new laboratory staff will be briefed on the content of the protocol, and the PI and staff certified understanding of the content of the protocol. The IACUC modified the animal incident reporting form to include all Veterans Affairs reporting requirements.

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.

Sincerely,

(B6)

for

(B6)

M.S., D.V.M.

Deputy Director

Office of Laboratory Animal Welfare

cc: IACUC Chair

(B6)

(B6)

D.V.M., Ph.D., VA Chief Veterinarian  
Ph.D., ORO

# Department of Veterans Affairs

# Memorandum

**Date:**

DEC 21 2018

**From:**

Director, Truman VA, Columbia, MO (DIR)

**Subj:**

Update-Protocol deviation; Delay in communicating a reportable incident; ORO Case # 589A4-0061-A

**To:**

Office of Research Oversight (ORO), Research Safety Animal Welfare Group  
Chief Veterinary Medical Officer (CVMO)  
Office of Laboratory Animal Welfare (OLAW)  
Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC).  
Network Director, VA Heartland Network

1. On Thursday, November 8, 2018, the Institutional Animal Care and Use Committee (IACUC) which is locally called the Subcommittee for Animal Studies (SAS) communicated to the Truman VA Medical Center Director a protocol deviation reportable under applicable federal standards. SAS's determination occurred on October 25, 2018. The communication from the SAS Chair to the Director occurred beyond the five-working day requirement, per VHA Handbook 1058.01, section 7(f)2. This is a follow-up report from the initial November 13, 2018 report regarding ORO Case # 589A4-0061-A. The updated text will be in *italics text* below in section 1f.

a. **Facility Name and Animal Welfare Assurance Number:** Harry S. Truman Memorial Veterans' Hospital (Truman VA); A3157-01

b. **Research Animal Component Of Research Protocol (ACORP)**  
**Title(s):** Mineralocorticoid Receptor Mediates Vascular Stiffness Via Dysregulated Immunity in Perivascular Adipose Tissue"

c. **Facility Number(s):** SAS ACORP #195 under research project  
(B6) [REDACTED] Project # 1

d. **Funding Source(s):** NIH K award # 1K08HL132012-01A1, Mentored clinical Scientist Research Career Development Award

e. **Detailed Description of the Event(s):** On October 3, 2018, the PI reported to SAS that he had infused 36 mice with Angiotensin (Ang) II at 500 ng/kg/day, a naturally occurring hormone, that was not an approved procedure for use on his ACORP #195. The PI reported the unapproved infusions occurred over three separate timepoints; September 2017: 17 mice; January 2018: 8 mice; June 2018: 11 mice. The PI reported mice that received the unapproved Ang II infusion were approved for use on ACORP #195. The PI attributed the error to staff confusion, specifically mixing up which protocol involved Ang II

procedure and current SAS approved procedures. The PI stated staff confusion occurred since the same mouse strains that were infused with Ang II on ACORP # 195 were also previously used on a collaborator's ACORP that was conducted in the same laboratory and by the same staff. Staff presumed that the Ang II was included on ACORP 195. The PI submitted a protocol deviation after a careful review of the PIs approved procedures and PI's discovery the procedure was unapproved.

**f. Detailed Description of the Actions Taken (or to be taken) to address the reported event, including systematic action(s) where warranted:** The PI submitted an amendment on October 9, 2018 to add the Ang II infusion procedure to ACORP #195. SAS approved the PIs amendment on October 25, 2018.

SAS deliberated the incident at their regular, fully convened meeting on October 25, 2018 and determined the incident was reportable to ORO, Office of Laboratory Animal Welfare (OLAW), and the Chief Veterinarian Medical Officer (CVMO), per VHA Handbook 1058.01, section 7(f)2 and written local policy. SAS also voted to require the PI submit a detailed corrective action plan (CAP) to ensure that protocols are managed appropriately and that staff are adequately informed of approved procedures on each protocol. The CAP is due to SAS by November 15, 2018.

The SAS Chair communicated to the Facility Director the above described incident as reportable on November 8, 2018. Because this work is partially supported by NIH funds and the grant is administered through the affiliate, the University of Missouri Animal Care Quality Assurance (ACQA) office were also be notified by SAS of their determination on that same date.

The SAS Chair's communication to the Medical Center Director occurred 10 working days after SAS's determination which was five days beyond the five-day reporting requirement in VHA Handbook 1058.01. The SAS Chair was educated on the reporting requirements by the RCO on November 8, 2018 when notified of SAS's determination. At their next scheduled meeting on November 29, 2018, the SAS Chair will provide education to the SAS membership regarding VHA 1058.01 and SAS procedures, as well as discuss the late reporting to the Facility Director to determine what mechanisms can be modified and used to ensure future timely reporting complaint with VHA 1058.01.

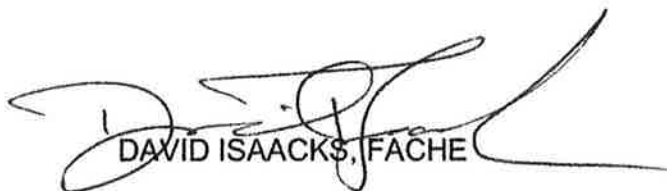
*Update as of December 10, 2018: On November 29, 2018 the fully convened SAS deliberated the PIs CAP (received prior to the SAS's deadline) and voted to accept the PIs CAP. The CAP stated actions that will occur to prevent future events included: (a) the PI and lab manager will discuss and verify with all involved personnel the accepted and appropriate procedures as they relate to current ACORP (prior to starting new experimental procedures, as well as regularly in lab meetings); (b) the ACORP will be maintained in electronic and printed form for ease of review by all personnel; (c) all future interventions in animals will require thorough review of the ACORP by the PI and senior staff*

prior to implementation; (d) all current and incoming personnel will be required to read and understand all aspects of an animal protocol for the responsible PI prior to any animal work by the individual; and (e) all personnel, including the PI, will be required to sign and date an attestation page indicating they have read and understand the ACORP. SAS also voted to close the matter on November 28, 2018 and send a communication to the PI.

On November 28, 2018, the SAS Chair also lead the discussion amongst the membership regarding strategies to avoid future non-compliance by SAS (e.g., late reporting to the Facility Director as outlined in VHA Handbook 1058.01). SAS voted to modify their Animal Incident Report Form to include all indicated reporting requirement language from VHA Handbook 1058.01 to allow the reporting requirements to be readily available to the reviewers and all SAS members. The form is currently being modified and will be on the next SAS agenda for their consideration, review, and finalization. The next scheduled SAS meeting is December 27, 2018 and will remain on future agendas until the form has been finalized and distributed to applicable research staff.

g. **External Agencies/Organizations Notified of the Event:** This update will be sent to the OLAW, CVMO, Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC), and the affiliate ACQA.

2. Please contact (B6) at (b) (6) if additional information is required.

  
DAVID ISAACKS, FACHE

(B6) (NIH/OD) [E]

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Wednesday, December 26, 2018 6:41 AM  
**To:** (B6) CMOVAMC  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: Follow-up Report of Non-compliance from Harry S Truman Memorial Veterans' Hospital (Truman VA); ORO Case #589A4-0061-A

Thank you for this report (B6) We will respond soon.

(B6) M.S., D.V.M.  
Deputy Director, OLAW

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**From:** (B6) L. CMOVAMC (B6) @va.gov>  
**Sent:** Friday, December 21, 2018 3:29 PM  
**To:** 'accredit@aaalac.org' <accredit@aaalac.org>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** (B6) @va.gov>; (B6) CMOVAMC  
(B6) @va.gov>  
**Subject:** Follow-up Report of Non-compliance from Harry S Truman Memorial Veterans' Hospital (Truman VA); ORO Case #589A4-0061-A

On behalf of the Medical Center Director, please find attached a follow-up report of non-compliance related to research occurring at the Harry S Truman Memorial Veterans' Hospital (Truman VA). An update has been provided. Let me know if you have any questions.

Happy Holidays to you and yours!

(B6)

(B6)

(B6)

Office of the Director  
Harry S Truman Memorial Veterans' Hospital (Truman VA)  
and  
Clinical Assistant Professor of Medicine and Psychiatry  
University of Missouri  
Columbia, MO 65201

(b) (6)

**Hippocrates:** *"Let food be thy medicine, and medicine be thy food."*

**Department of  
Veterans Affairs****Memorandum**

**Date:** NOV 13 2018  
**From:** Director, Truman VA, Columbia, MO (DIR)  
**Subj:** Protocol deviation; Delay in communicating a reportable incident  
**To:** Office of Research Oversight (ORO), Research Safety Animal Welfare Group  
Chief Veterinary Medical Officer (CVMO)  
Office of Laboratory Animal Welfare (OLAW)  
Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC).  
Network Director, VA Heartland Network

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same laboratory and by the same staff. Staff presumed that the Ang II was included on ACORP 195. The PI submitted a protocol deviation after a careful review of the PIs approved procedures and PI's discovery the procedure was unapproved.

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2. Please contact (B6) at (b) (6) if additional information is required.

  
DAVID ISAACKS, FACHE

(B6) [REDACTED] (NIH/OD) [E]

**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Wednesday, November 14, 2018 12:27 PM  
**To:** (B6) [REDACTED] CMOVAMC; OLAW Division of Compliance Oversight (NIH/OD)  
**Cc:** (B6) [REDACTED] CMOVAMC; (B6) [REDACTED] CMOVAMC  
**Subject:** RE: Initial Report of Non-compliance from Harry S Truman Memorial Veterans' Hospital (Truman VA)

Thank you for providing this preliminary report. We will open a case file and await the update as noted in your email.

Best regards, (B6) [REDACTED]

(B6) [REDACTED] DVM, DACLAM  
Director  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health

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**From:** (B6) [REDACTED] L. CMOVAMC [mailto:(B6) [REDACTED]@va.gov]  
**Sent:** Wednesday, November 14, 2018 11:33 AM  
**To:** accredit@aaalac.org; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** (B6) [REDACTED] CMOVAMC <(B6) [REDACTED]@va.gov>; (B6) [REDACTED] CMOVAMC <(B6) [REDACTED]@va.gov>  
**Subject:** Initial Report of Non-compliance from Harry S Truman Memorial Veterans' Hospital (Truman VA)

On behalf of the Medical Center Director, please find attached an initial report of non-compliance related to animal research occurring at the Harry S Truman Memorial Veterans' Hospital (Truman VA). An update will be provided following further deliberation of the animal care and use committee as outlined in the attached report. Let me know if you have any questions.

(B6) [REDACTED]

(B6) [REDACTED]  
(B6) [REDACTED]  
Office of the Director  
Harry S Truman Memorial Veterans' Hospital (Truman VA)  
and  
Clinical Assistant Professor of Medicine and Psychiatry  
University of Missouri  
Columbia, MO 65201  
(b) (6) [REDACTED]

**Hippocrates:** *"Let food be thy medicine, and medicine be thy food."*