

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

March 7, 2019

Re: Animal Welfare Assurance
A4365-01 [OLAW Case 3V]

Dr. Stephan Monroe
Associate Director for Laboratory
Science and Safety
Centers for Disease Control
1600 Clifton Road NE, (b)(6)
Atlanta, GA 30333

Dear Dr. Monroe,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 6, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Centers for Disease Control and Prevention. According to the information provided, OLAW understands that a rabbit serving as a host for feeding ticks became pale and dehydrated after a greater number of ticks was placed on the animal than approved in the protocol. Also, this rabbit was of a lesser body weight for the load of ticks applied. Following implementation of corrective actions, this same issue was repeated and again involved the use of underweight rabbits infested with a larger tick load than approved.

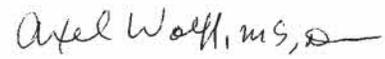
The initial corrective actions consisted of removing 1/3 of the ticks and providing supportive care which led to gradual recovery of the rabbit. The rabbit was subsequently euthanized in accordance with the protocol. The Institutional Animal Care and Use Committee (IACUC) directed the Principal Investigator (PI) to amend the protocols involved, to have the PI and staff certify understanding of the content of the protocol, to have the Comparative Medicine Branch monitor the Packed Cell Volumes of all rabbits hosting ticks, to use only the number of ticks per body weight as approved in the protocol, to record information in the clinical record regarding vitamin supplementation, tick infestation numbers, animal weights, bleeding volumes and site, and euthanasia details. The clinical information must also be included in future protocol renewals.

Following the second incident, the PI was directed to stop the animal activities and have the veterinary staff take care of the rabbits. Additional corrective actions were implemented and consisted of adding a co-PI to the study for additional oversight, having all protocol staff certify understanding of the content of the protocol before starting work, assessing competency of staff and maintaining training records, developing standard operating procedures (SOP) which must be approved by supervisors, and training staff on the SOPs. The protocol suspensions will remain in effect until the amendments are approved by the IACUC.

Based on its assessment of these explanations, 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 and recommends that this study be placed under enhanced post-approval monitoring. Thank you for informing OLAW about this matter.

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Sincerely,



Axel Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare

cc: Chief, Animal Care and Use Program Office



4365-3V

PHS Assurance# A4365-01

6 March 2019

Dr. Brent Morse
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive – MSC 7982
Bethesda, MD 20892-7982
Via email: olawdco@od.nih.gov

Dear Dr. Morse,

On 21 December 2018, the Attending Veterinarian (AV) notified the CDC Atlanta IACUC Chairperson and Animal Care and Use Program Office (ACUPO) Chief of an incident involving a rabbit. This incident was further discussed at the IACUC meeting that was held on 7 January 2019. Comparative Medicine Branch (CMB) veterinarians described to the committee that a health notification was sent to veterinary residents regarding a rabbit that had been infested with ticks on 10 December 2018 and was presenting on 14 December 2018 as pale and dehydrated. Three bags were found on the animal containing a reported 70 pairs of adult ticks. Supportive care was immediately provided and, after several days of continued supportive care and removal of approximately one third of the ticks, the animal showed some signs of improvement. On 18 December 2019, the program elected euthanasia for the animal as it was the end of the study. Records showed that the rabbit weighed 3.10 kg on 30 November 2018 and 2.96 kg on 18 December 2018.

According to protocol, two bags are to be placed on animals weighing at least 3.5 kg, while in this instance, three bags were placed on an animal weighing less than 3.5 kg. After further discussion during the IACUC meeting held on 4 February 2019, the committee voted to report this incident to OLAW as a protocol non-compliance. At that time, the committee required that the following corrective actions be taken:

- 1) The Principal investigator (PI) must submit an amendment to both protocols involving tick placement on rabbits containing the modifications requested by the committee.
- 2) Once the amended protocols receive IACUC approval, the PI and all associates must read and understand them, provide signatures to document this re-training on an ACUPO training form, and submit the form to the ACUPO office.
- 3) CMB will provide weekly Packed Cell Volume (PCV) monitoring of all rabbits during periods of tick infestation.

- 4) The PI must ensure that the number of bags and ticks that are placed on each animal does not exceed the maximum stated in the protocol, based on the weight of that particular animal.
- 5) All animal interactions must be documented in clinical records, including but not limited to:
 - a) Vitamin B supplementation (including whether dietary or injection [dose and site])
 - b) Infestations (including animal weight, number of bags and ticks placed on each animal)
 - c) All bleeding events (including animal weight, volume, and site of collection)
 - d) Euthanasia (dose, site of administration)
- 6) The PI must include these documentation practices in all future renewals of these protocols.

On 22 February 2019, the Post Approval Monitoring (PAM) officer discovered a repeat incident when protocol associates were observed placing bags of ticks onto four rabbits. Two of the rabbits weighed 2.6 kg and one of the rabbits had three bags placed onto it. As described above, the IACUC had previously informed the PI for this protocol that these practices were a non-compliance of both protocols. At that time, the PI was cited for the infraction, and was required to amend the protocols accordingly.

Immediately following this second incident, the AV and IACUC Chairperson instructed the PI to stop the animal activities under these protocols until the welfare of the animals can be assured and continuation of activities are approved by the CDC Atlanta IACUC. All affected animals are being closely monitored by CMB veterinary staff and have been provided husbandry and treatment as needed.

In addition, a meeting was held with the PI's supervisor and Branch Chief, the IACUC Chairperson, the AV and Deputy Chief Veterinarian, and ACUPO Chief, to discuss these incidents, how to best prevent non-compliances in the future, and how to assure the welfare of these animals.

The Branch Chief is instituting the following corrective actions:

- 1) IACUC protocols
 - a. A Co-PI will be added to all protocols to ensure all administrative requirements are met, and met in a timely manner.
 - b. All protocol personnel will sign-off that they understand the contents of the approved protocol prior to beginning work on that protocol.
- 2) Training
 - a. The Branch quality manager will maintain training records for all animal protocol staff, which will include a training checklist of experience and competency requirements needed for new staff to work independently. Also, protocol staff will be assessed annually for competency in animal procedures.
- 3) Standard Operating Procedures (SOPs)

- a. SOPs will be created for all routinely-performed procedures, which will be reviewed and approved by the Direct Supervisor and Branch-level Quality Manager.
- b. All animal protocol staff will be trained on these SOPs with refresher trainings conducted annually.

The CDC Atlanta IACUC discussed this second incident at the meeting that was held on 4 March 2019 and the Committee was in support of the corrective actions described above and the temporary suspension of both protocols until amendments to the protocols are approved by the IACUC. In addition to the first incident, the committee voted to report this second incident and the temporary suspension of protocols to the Office of Laboratory Animal Welfare (OLAW).

CDC takes its stewardship of the animals in its care extremely seriously. We continually strive to assure that the highest standards possible are followed to help ensure that animals are treated and cared for in a humane manner.

Thank you for your consideration of this matter.

Sincerely,

(b)(6)

3/6/2019

X *Stephan S. Monroe*

Stephan S. Monroe, PhD
Institutional Official
Signed by: PIV

Stephan S. Monroe, PhD
Institutional Official
Director, Office of Laboratory Science and Safety

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, March 7, 2019 6:42 AM
To: Monroe, Steve (CDC/DDPHSS/OLSS/OD)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: PHS Assurance# A4365-01; Notification of non-compliance and corrective actions

Thank you for this report, Dr. Monroe. We will send a response soon.

Axel Wolff, M.S., D.V.M.
Deputy Director, OLAW

From: Monroe, Steve (CDC/DDPHSS/OLSS/OD) (b)(6)
Sent: Wednesday, March 6, 2019 4:22 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Animal Care and Use Program Office (CDC) (b)(6)
(b)(6)
Subject: PHS Assurance# A4365-01; Notification of non-compliance and corrective actions

Dr. Morse and colleagues,

Attached please find a letter describing a non-compliance at a CDC Atlanta facility and the follow-up actions recommended by the IACUC and implemented by program leadership.

Please contact me if you have any questions or require additional information.

Best,
Steve

Steve Monroe, PhD
Institutional Official
Associate Director for Laboratory Science and Safety
Centers for Disease Control and Prevention (CDC)

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OLSS Office of Laboratory
Science and Safety
Strengthening the culture of laboratory science and safety at CDC