



DEPARTMENT OF HEALTH & HUMAN SERVICES

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NATIONAL INSTITUTES OF HEALTH

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Office of Laboratory Animal Welfare
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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) 480-3387

April 6, 2022

Re: Animal Welfare Assurance
#A3125-01 (OLAW Case V)

Dr. Maria T. Zuber
Vice President for Research
Massachusetts Institute of Technology
77 Massachusetts Ave., (b) (4)
Cambridge, Massachusetts 02139

Dear Dr. Zuber,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 21, 2022 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals within the animal care and use program at the Massachusetts Institute of Technology (MIT). Your letter supplemented the information contained in an initial telephone report to this office on January 7, 2022. According to the information provided, OLAW understands that a rhesus macaque sustained an injury during a Committee on Animal Care (CAC)-approved research activity supervised by two laboratory personnel. The laboratory members moved the macaque to a chair for study purposes, using a collar to control the animal. The animal became agitated in the chair and threw his weight against the collar. The laboratory members did not know how to properly intervene and did not recognize that an injury occurred. The incident was not reported to veterinary staff. After the incident, veterinary staff observed during routine rounds that the macaque had bruising around both eyes and scleral hemorrhages. Upon sedation, bruising in the mouth was found which was consistent with pressure on the neck from the collar. The collar was removed and the macaque has fully recovered from the injury. The animal involved in this incident was supported by funds from the Office of Naval Research and the National Science Foundation (NSF).

The CAC investigated the matter and concluded that the incident represented a programmatic deficiency in research personnel training, specifically in the basics of training an inexperienced macaque to a chair, how to respond to unexpected situations when working with macaques, and when to contact veterinary personnel.

Several corrective and preventive measures were implemented. The responsible laboratory members agreed not to work with animals outside of their enclosures pending retraining and CAC review. The responsible laboratory members' retraining will include prompt veterinary consultation and proper handling of macaques during chairing procedures. Two trainers were designated within the laboratory who will work with the Division of Comparative Medicine (DCM) to ensure proper training of new macaques, and training procedures and equipment will be modified to minimize risk to the animals.

Measures will also be initiated institution-wide to ensure proper macaque chair training procedures. Training sessions will cover animal training techniques, recognition of pain and distress, and seeking appropriate veterinary attention for animals. Representative trainers from each laboratory will meet with DCM to review their training goals and training procedures. The DCM veterinarian or behaviorist will ensure competency of each individual trainer. Finally, going forward, all laboratory members working with macaques will attend annual nonhuman primate refresher courses and animal training sessions will be subject to triennial observations by DCM behavior or veterinary personnel. There will also be enhanced oversight of all laboratory members new to training macaques and of training techniques used for macaques naïve to chairing studies.

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OLAW Case A3125-V

OLAW appreciates the consideration of this matter by MIT, which was consistent with the philosophy of institutional self-regulation. Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate this incident and prevent recurrence. We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

Robyn M. Engel -S

Digitally signed by Robyn M.
Engel -S
Date: 2022.04.06 11:26:35 -04'00'

Robyn M. Engel, DVM
Animal Welfare Program Specialist
Office of Laboratory Animal Welfare

cc: IACUC contact

Dr. Robert M. Gibbens, USDA, APHIS, Animal Care
Edda Thiels, NSF Animal Welfare Officer



Date: 03/21/2022

To: Axel Wolff, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360
6705 Rockledge Drive
Bethesda, MD 20892

From: Dr. Maria T. Zuber, Institutional Official, Vice President for Research at MIT

cc: Dr. Kelly Metcalf Pate, Associate Professor and Director of the Division of
Comparative Medicine (DCM), Attending Veterinarian
Dr. Howard Heller, Chair of Committee on Animal Care (CAC)
(b) (6)
AAALAC, International

Re: Reportable program deficiency under PHS Assurance A3125-01 in accordance
with PHS Policy IV.F.3

Dear Dr. Wolff,

We write to report a deviation from the provisions of the PHS Policy and Guide. Drs. Pate and Heller made a preliminary report by phone to you on 01/07/22 concerning an injury to a macaque that occurred during CAC-approved research activities under protocol number 1219-075-22 titled "Neuronal Mechanisms Underlying Visual Object Recognition" that revealed this deviation. The USDA was notified on 01/11/22 by Drs. Pate and Heller per OLAW recommendation.

Explanation of incident:

On 12/07/21 a rhesus macaque (*Macaca mulatta*) sustained an injury from his collar while working in a research lab on CAC-approved research activities under the supervision of two lab personnel. The incident was not reported to veterinary personnel at that time, and on 12/09/21 the macaque was observed to have bruising around both eyes and scleral hemorrhages by DCM veterinary staff during routine rounds. The animal was provided with veterinary care, including analgesia, at that time, and the lab was contacted. When questioned, lab members recounted that the animal had become agitated in his chair in the lab two days prior and threw his weight against his collar during that time. At that time, veterinary staff requested that the two lab members who had been present for the incident not handle animals until further discussion and the lab members

agreed. The macaque was observed for neurological issues, and then sedated for an exam on 12/10/21 which confirmed the enclosure-side observations and found bruising in his mouth consistent with pressure on the neck from the collar. The collar was removed at that time and the macaque has since fully recovered from the injury.

On 12/10/21 the Attending Veterinarian and a DCM staff veterinarian met with the PI and the two lab personnel who were present for the incident. The lab members shared that they were not sure how to intervene when the incident occurred and did not recognize at the time that injury occurred during the incident. They agreed that the two personnel who were present for the incident would voluntarily stop doing work with animals outside of their enclosures to allow for CAC review of the events and a period of retraining. The Attending Veterinarian and DCM staff veterinarian informed the CAC of the incident on 12/10/21 following this discussion.

Corrective and preventative actions:

The CAC Chair and the CAC Program Manager met with the PI and the two lab personnel on 12/16/21 to discuss the incident, and the CAC discussed the incident at convened meetings on 01/13/22, 01/21/22, and 02/03/22. The CAC concluded that the incident represented a programmatic deficiency in research personnel training, specifically in the basics of training an inexperienced macaque to chair, how to respond to unexpected situations when working with macaques, and when to contact veterinary personnel. The CAC approved two courses of corrective and preventative action:

1. Plan #1: A re-training plan to allow the lab personnel involved in this incident to resume independent research activities with macaques. (Approved 01/21/22)
2. Plan #2: An institution-wide training plan to ensure that all current and future macaque users are properly trained to work with macaques. (Approved 02/03/22)

Details of each plan are as follows:

Plan #1: to allow DiCarlo Lab Personnel to resume training activities with macaques:

1. Retraining of the two lab members involved in the incident started on 12/13/21 and is ongoing. Lab members agreed to not work with any macaques outside of enclosure without direct observation by DCM personnel pending official sign-off. Review of the final approved plan occurred with the PI on 02/03/22 and with the involved lab members on 02/17/22.

2. To ensure prompt veterinary consultation (Timeline: to occur prior to sign-off for independent training – this meeting occurred on 02/15):
 - Lab personnel meet with DCM personnel to discuss what to look out for to identify “worst case scenarios” in chair training and appropriate immediate action.
 - Emphasize the need to consult a veterinarian when unexpected occurrences happen.
3. To ensure proper training (Timeline: Effective immediately):
 - For working with already trained macaques:
 1. For lab personnel who were involved in the incident, chairing procedures will be observed by DCM personnel knowledgeable in animal behavior until DCM personnel feel confident to sign off on work with each macaque.
 2. For lab personnel not involved in the incident, the procedures for all research personnel who work with macaques should be followed (Plan #2).
 - Prior to training the macaque involved in the incident and other new macaques specifically:
 1. The lab has designated two trainers within the laboratory who will be authorized to do chair training with new macaques who are naïve to training. Trainers will require DCM staff sign-off prior to working with new macaques outside of home cage.
 2. These two trainers will be mentored by an experienced trainer from another lab (TBD) and DCM personnel as that experienced trainer trains a naïve macaque. This process is expected to take 1-2 months.
 3. Following that process, DCM personnel will work with these trainers to train the macaque involved in this incident and other naïve animals. DCM personnel will work with the lab to create a shaping plan and training record to document all training sessions and will sign off on training plans before implementation by lab, with defined nodes that will require reassessment. DCM personnel will watch the training process in full for at least one naïve macaque for both trainers.
4. To ensure all procedures and equipment minimize risk (Timeline: TBD):

- Change from chain to yoke style collars for all future macaques, and as feasible all macaques who are currently collared.
- All naïve animals will attempt collarless chairing prior to receiving a collar.
- Modify chair from a top-loading to side-loading door.

Plan #2: to ensure proper macaque chair training procedures for all macaque users institution-wide:

To implement for all macaque users within the first half of 2022 without interrupting current study flow unless a problem occurs:

1. Zoom or in person didactic training session for each lab that will cover:
 - a. the basic tenets of training
 - b. how to recognize factors that may lead to animal distress or injury
 - c. how to recognize an animal in active distress and appropriate action to take
 - d. the appropriate circumstances and timeline in which to seek veterinary attention for animals
2. Meeting with a representative trainer with or without the PI of each lab to review general chair training procedures to have lab:
 - a. discuss the goals of the lab and the training, and
 - b. review chair training procedures and demonstrate the ideal procedure.
 - c. After review, DCM may suggest updates or changes to improve procedures and/or equipment where animal or personnel safety are at risk. Standard chairing procedures for the lab will be documented in writing. Any disagreements between DCM and the lab regarding the need for updates or changes will be reviewed by the CAC.
3. Ensure competency of each individual trainer within the lab in working with all currently assigned macaques:
 - a. Direct observation of training practices and sign-off by DCM veterinarian or behaviorist. Depending on the experience and demonstrated competency of the individual trainer, this may be required for only one select macaque assigned to that trainer, or for all macaques assigned to that trainer. Similarly, depending on the experience and demonstrated competency, more than one observation session may be needed.

Going forward, all lab members currently working with macaques will undergo (Timeline: Effective immediately):

1. Yearly “NHP refresher” course for all personnel working with NHPs. Lack of compliance with this requirement by the yearly deadline will result in loss of facility access.
2. Triannual observations by DCM behavior / veterinary personnel of a training session for each macaque to ensure that training procedures don't drift and preemptively identify problem areas, with documentation. These can occur concurrent with headcap maintenance checks.

All lab members new to training macaques will undergo (Timeline: Effective immediately):

1. Preliminary interview to identify level of baseline knowledge, with a didactic training session as outlined above.
2. Direct observation and assessment of comfort level of training, with all training sessions requiring observation by DCM personnel or a DCM-approved lab training mentor until sign-off by DCM personnel.

For all macaques naïve to training (Timeline: Effective immediately):

1. DCM will observe in home cage and evaluate training strategies based on personality and tasks needed to be performed.
2. DCM will work with the researchers to design a shaping (training) plan for animal and discuss with lab on how to execute the plan.
 - a. DCM will be present for all training sessions until there is evidence of affiliative/cooperative behavior between trainer/monkey for at least three consecutive sessions.
 - b. Shaping plans may include specific “nodes” at which a macaque will require DCM observation and sign-off prior to progressing to the next stage of training.
3. All use of a collar and types of collars for individual macaques must be approved by DCM prior to implementation. Labs must attempt to train an animal to chair without a collar, or scientifically justify the need for a collar in their CAC protocol, before use of a collar will be approved by DCM. If a collar is deemed necessary to facilitate training for a macaque, macaques must be fully acclimated to the collar as assessed by DCM staff prior to the start of training that uses the collar as a training tool.

Following any incidences where an unexpected event occurs during a training procedure that may have resulted in stress and/or injury to the animal (Timeline: effective immediately):

1. A veterinarian will be contacted as soon as practical to assess the situation



2. All training/water restriction will temporarily cease until veterinarian and behavioral personnel agree that training may resume. Should the unexpected event require CAC review, the CAC may further deem that training not resume until after review of the case by the committee.

Confirm no other active potential areas of concern (Timeline: to complete by the end of 2022):

1. Review a summary of all reports of morbidity and mortality of macaques for past year to ensure no patterns.
2. Reassess current practices for training / oversight of other high-risk areas:
 - Surgery
 - Implant maintenance

Funding source and impact on PHS-supported activities:

Animal research activities for this lab are supported by the Office of Naval Research (ONR) 60744752-114407 and N00014-20-1-2589, and the National Science Foundation BCS-2124136.

Though this incident did not involve any PHS-supported research activities, the aim of Plan #2 above is to ensure that no future incidents occur that could impact PHS-supported activities in a manner that will have a minimal impact on the progress of ongoing PHS-supported activities.

We trust that OLAW will find our response to this incident and our plan to address the noted programmatic deficiency adequate. Please inform me or Drs. Pate or Heller if you need further clarification.

Regards.

Maria T. Zuber

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, March 23, 2022 7:30 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Deviation from PHS Policy and Guide at MIT (A3125-01)

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

From: (b) (6)
Sent: Monday, March 21, 2022 7:06 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Kelly Metcalf Pate <kpate@mit.edu>; Howard M Heller <hheller@mit.edu>; (b) (6)
accredit@aaalac.org
Subject: [EXTERNAL] Deviation from PHS Policy and Guide at MIT (A3125-01)

CAUTION: This email originated from outside of the organization. Do not click links or open attachments unless you recognize the sender and are confident the content is safe.

To Whom it May Concern,

Please find attached a memo signed by our IO, Dr. Maria T Zuber, regarding a deviation from the provisions of the PHS Policy and Guide identified at MIT (PHS Assurance A3125-01, AAALAC unit 000191), as preliminarily reported to Dr. Axel Wolff by Drs. Kelly Metcalf Pate and Howard Heller on 1/7/22.

Thanks,

(b) (6)



Initial Report of Noncompliance

By: (b)(6)

Date: 1/7/22

Time: 400

Name of Person reporting: Kelly Pate DVM, Howard Heller I have chosen
Telephone #: (b)(6)
Fax #:
Email:

Name of Institution: MIT
Assurance number: A3125

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

What happened?
Monkey being trained to chain had collar too tight + was agitated. Lab didn't release chain + monkey sustained injury. Eyes swollen. Staff inexperienced. Staff not knowledgeable about positive reinforcement.
Species involved: Rhesus
Personnel involved: Lab staff
Dates and times:
Animal deaths:

Projected plan and schedule for correction/prevention (if known):
Retrain lab staff how to do training.
Monkey recovered. Reassess training of staff working w/ primates. Modify chaining procedures.

Projected submission to OLAW of final report from Institutional Official:

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