

Wolff, Axel (NIH/OD) [E]

From: Ward, Joan (NIH/OD) [E]
Sent: Thursday, March 29, 2018 6:43 AM
To: Wolff, Axel (NIH/OD) [E]
Subject: FW: OLAW Case A3111-G

FYI

From: Nestler, Eric [mailto:eric.nestler@mssm.edu]
Sent: Wednesday, March 28, 2018 7:00 PM
To: Ward, Joan (NIH/OD) [E] <wardjoa@od.nih.gov>
Cc: IACUC <IACUC@mssm.edu>; Gibbens, Robert - APHIS (Robert.M.Gibbens@aphis.usda.gov)
<Robert.M.Gibbens@aphis.usda.gov>; Martinelli, Giorgio <giorgio.martinelli@mssm.edu>
Subject: Re: OLAW Case A3111-G

Joan,

Please thank Dr. Wolff for his formal response. We did want to assure him that Bronx VA personnel were part of the investigation from the very beginning, and that the VA remains fully informed of the findings and outcome.

Best,

Eric Nestler

From: "Ward, Joan (NIH/OD) [E]" <wardjoa@od.nih.gov>
Date: Wednesday, March 28, 2018 at 8:08 AM
To: "Nestler, Eric" <eric.nestler@mssm.edu>
Cc: IACUC <IACUC@mssm.edu>, "Gibbens, Robert - APHIS (Robert.M.Gibbens@aphis.usda.gov)"
<Robert.M.Gibbens@aphis.usda.gov>
Subject: OLAW Case A3111-G

Dear Dr. Nestler,

Attached please find Dr. Axel Wolff's final response to OLAW Case A3111-G.

If you have any questions, feel free to contact us by phone or by email.

Regards,
Joan

*Joan Ward
Program Specialist
Office of Laboratory Animal Welfare
National Institutes of Health
6705 Rockledge Drive, Suite 360
Bethesda, MD 20892
301-594-2506
wardjoa@od.nih.gov*



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

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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
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Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

March 27, 2018

Re: Animal Welfare Assurance
#A3111-01 (OLAW Case G)

Eric Nestler, M.D., Ph.D.
Dean for Academic Affairs
Icahn School of Medicine at Mount Sinai
Icahn Building (b) (4)
1425 Madison Avenue
New York, NY 10029-6574

Dear Dr. Nestler,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your February 16 and March 22, 2018 letters reporting two instances of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Icahn School of Medicine at Mount Sinai (ISMMS), following up on an initial report on January 11, 2018. According to the information provided, OLAW understands the following about the incidents and the corresponding corrective actions:

- 1) A nonhuman primate died after receiving an accidental overdose of an approved experimental drug. A calculation error in drug preparation led to this outcome.

Corrective action: The laboratory and veterinary staff immediately performed cardio-pulmonary resuscitation but the animal still died. The Principal Investigator and staff will now consult with the veterinarians regarding drug dosages prior to administration to the monkeys.

- 2) Thirty eight mice had been transported without authorization from a Veterans Affairs facility to ISMMS. The introduction of foreign mice into the facility constituted a biosafety risk to the in-house colony and there was also concern about the containers and vehicle used as well as the safety of the mice. The Principal Investigator (PI) personally transported the mice with help from a technician but initially failed to admit it. The mice were not harmed in this incident.

Corrective action: The PI was assigned a mentor who will provide monitoring and counseling, the PI and laboratory staff were retrained and the laboratory was placed on enhanced post-approval monitoring, the PI was placed on probation, and the PI and staff must be escorted into the vivarium. The PI must submit periodic research status reports to the Institutional Animal Care and Use Committee (IACUC) and she was warned about the consequences of future noncompliance.

Based on its assessment of these explanations, OLAW understands that measures have been implemented in both situations to correct and prevent recurrence of the problem. OLAW concurs with the actions taken by the IACUC to comply with the PHS Policy and recommends that the James J. Peters Bronx VA Hospital IACUC also be informed about the unauthorized animal transfer to ensure that animals are not being inappropriately discharged. We appreciate having been informed of these matters and find no cause for further action by this Office.

Page 2 – Dr. Nestler
March 27, 2018
OLAW Case A3111-G

Sincerely, *

(b) (6)

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

cc: IACUC Chair
Robert Gibbens, D.V.M., USDA-APHIS-AC



Icahn School of Medicine at Mount Sinai

IACUC
One Gustave L. Levy Place, Box 1155
New York, NY 10029
Tel: (212) 241-0153
Fax: (212) 241-5550
Email: IACUC@mssm.edu

March 22, 2018

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

Dear Dr. Wolff:

The Icahn School of Medicine at Mount Sinai (ISMMS) Institutional Animal Care and Use Committee (IACUC), in accordance with its Assurance D16-00069 (A3111-01), PHS Policy IV.F.3., and NIH Guide Notice NOT-OD-05-034 submits this report of noncompliance regarding an incident of unauthorized animal importation related to protocols, ISMMS GCO number 17-0288 (NIH AG057440-01), 14-0141 (R01 AG048923-01), PI: Dongming Cai, M.D., PhD, Associate Professor, Department of Neurology. This incident was first reported to OLAW on January 11, 2018 via telephone and e-mail by (b) (6)

Impact on PHS-supported activities: There were no potential or actual effects on PHS-supported activities.

Compliance with terms and conditions: No unallowable costs were charged during the non-compliant period.

Animal Harm: No harm came to the animals.

Description of the incident:

On September 26, 2017, a Vivarium manager observed a person carrying a large parcel going from the Vivarium toward the passenger elevators in the Annenberg Building of the ISMMS. Suspecting that the parcel contained animals about to be transported on passenger elevators (strictly prohibited by institutional rules), the supervisor intercepted the person. The person identified herself as a technician working for Dr. Dongming Cai, a researcher in the department of Neurology of the ISSMS with a dual appointment at the James J. Peters Bronx VA Hospital (VA). After ascertaining that the parcel contained empty mouse cages, the manager asked why the technician was taking them to the laboratory. Due to inconsistencies in her explanations, the Manager called the Vivarium Assistant Director and both accompanied the technician to Dr. Cai's laboratory to interview the PI. After entering the laboratory, they discovered 38 mice in 15 animal transfer buckets with VA identification cards attached to them. Since it appeared that the mice had been transferred without authorization, the Director and the Associate Director of the Vivarium were also called in to interview the PI.

During the interview, Dr. Cai was asked about the source of the mice and how the mice arrived at ISSMS. Dr. Cai responded by claiming that she was unaware that the animals had been taken from

the VA facilities and transported to ISMMS campus without authorization. She also placed the entire responsibility for the incident on her staff. The Vivarium Director ordered that the mice be placed in quarantine until the incident was reported to and investigated by the IACUC.

A report about the incident filed by the Vivarium Director was presented to the IACUC at a convened meeting. The IACUC agreed that an investigation was warranted, since the incident had a variety of compliance violations (e.g. safety and biosafety of the transported animals, unclear means of conveyance, lack of transfer authorizations, and unauthorized introduction of animal in the ISMMS Vivarium with potential threat to the safety of the biosafety of animal colony at ISMMS). Furthermore, the statement by Dr. Cai attributing full responsibility for the incident to her staff did not seem tenable and needed to be investigated. The IACUC Chair appointed a subcommittee consisting of three IACUC members and a representative of the legal office of the ISMMS. The subcommittee was charged to pursue a confidential inquiry according to the procedures set forth in the ISMMS IACUC policy on non-compliance investigation. Dr. Cai was informed of the decision and had no objection to the composition of the subcommittee; the Institutional Official (IO) was also briefed by the IACUC Chair for the duration of the inquiry.

After interviewing witnesses, the PI's staff and the PI, it became clear that Dr Cai's assertions that she had no role in the incident were false. She ultimately admitted that she had taken the mice from the VA and transported them in her private car to the ISMMS laboratory with the help of her technician. She expressed regrets at the subterfuge, misleading accounts of facts and lies and assumed full responsibility for the incident. The subcommittee prepared a report, which was discussed and approved by the IACUC at a convened meeting. Dr. Cai was allowed to review the report and comment in writing on it. The report, which also contained IACUC recommendations regarding sanctions to the PI, was then forwarded to the IO.

The IO concurred with the findings and approved the sanctions. The proposed sanctions are: 1) The ISMMS would appoint a mentor to counsel and monitor Dr. Cai's professionalism as a PI and head of a laboratory, 2) Dr. Cai would be referred to the NIH program "*Professionalism and Integrity in Research Program*" 3) The PI would be on probation for one year, 4) Her Lab at the ISMMS would be subject to frequent periodic unannounced inspections, 5) The PI and her staff would be allowed only escorted entry into the vivarium, 6) Dr. Cai and her staff would have to take classroom and on line courses on global aspects of research, institutional policies, and federal and state regulations. 7) Dr. Cai would provide quarterly reports to the IACUC on her research activities. 8) Should Dr. Cai be found to engage in any activity non-compliant with Institutional or IACUC policies, she would be subject to further discipline up to and including termination.

The ISMMS and the IACUC are committed to protecting the welfare of animals used in research and appreciates the continued guidance and assistance provided by OLAW in this regard. Should you have any questions on this report please contact me.

Sincerely,

Eric Nestler

Digitally signed by Eric Nestler
DN: cn=Eric Nestler, o, ou,
email=eric.nestler@mssm.edu, c=US
Date: 2018.03.26 09:08:20 -05'00'

Eric Nestler, M.D., Ph.D.
Dean for Academic Affairs
Icahn School of Medicine at Mount Sinai,
Icahn Building (b) (4)
1425 Madison Avenue
New York, NY 10029
eric.nestler@mssm.edu
(b) (6)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, March 26, 2018 2:14 PM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Final Report from Icahn School of Medicine at Mount Sinai- Dongming Cai

Thank you. I will send a response to the IO soon.
Axel Wolff

From: (b) (6)@mssm.edu]
Sent: Monday, March 26, 2018 2:05 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: RE: Final Report from Icahn School of Medicine at Mount Sinai- Dongming Cai

From: (b) (6)
Sent: Monday, March 26, 2018 11:06 AM
To: 'Wolff, Axel (NIH/OD) [E]'
Subject: [Secure] RE: Final Report from Icahn School of Medicine at Mount Sinai- Dongming Cai

To: Dr. Axel V. Wolff, MS, D.V.M, Director of OLAW

Dear Dr. Wolff,

On behalf of the Icahn School of Medicine at Mount Sinai IACUC and the Institutional Official Dr. Eric Nestler, this email serves as a final report of the reportable incident of unauthorized transport of animals:

- 1 Unauthorized transport of animals:** Noncompliance issue related to unauthorized importation of mice. No harm came to the mice. This incident has been comprehensively investigated by the IACUC. The IACUC is in the processes of filing a final report to the I.O. The IACUC is recommending to the IO remedial actions but does not have a final plan yet.
Related to Protocols: ISMMS GCO numbers 17-0288 (NIH AG057440-01) 14-0141(R01 AG048923-01), and 13-1681-00001-01-PD (Alzheimer's Association).
PI: Dr. Dongming Cai
Funding Source(s) History: Internal department funding, NIH and Alzheimer's Disease

If you require further information please contact the IACUC Chair, Dr. Giorgio Martinelli @ (b) (6)
(b) (6) giorgio.martinelli@mssm.edu

Best regards,

(b) (6)

(b) (6)



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Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, March 26, 2018 3:21 PM
To: (b) (6) 'olawdco@od.nih.gov'
Subject: RE: RE: Final Report from Icahn School of Medicine at Mount Sinai- Dongming Cai-corrected email language

Thank you for the corrected email content. I will forward this message to Dr. Wolff.

Sincerely, Brent Morse

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

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From: (b) (6) @mssm.edu]
Sent: Monday, March 26, 2018 2:58 PM
To: 'olawdco@od.nih.gov'
Subject: FW: RE: Final Report from Icahn School of Medicine at Mount Sinai- Dongming Cai-corrected email language

Correction of email content. Final plan attached.

From: (b) (6)
Sent: Monday, March 26, 2018 2:05 PM
To: 'olawdco@od.nih.gov'
Subject: RE: Final Report from Icahn School of Medicine at Mount Sinai- Dongming Cai

From: (b) (6)
Sent: Monday, March 26, 2018 11:06 AM
To: 'Wolff, Axel (NIH/OD) [E]'
Subject: [Secure] RE: Final Report from Icahn School of Medicine at Mount Sinai- Dongming Cai

To: Dr. Axel V. Wolff, MS, D.V.M, Director of OLAW

Dear Dr. Wolff,

On behalf of the Icahn School of Medicine at Mount Sinai IACUC and the Institutional Official Dr. Eric Nestler, this email serves as a final report of the reportable incident of unauthorized transport of animals:

- 1 **Unauthorized transport of animals:** Noncompliance issue related to unauthorized importation of mice. No harm came to the mice. This incident has been comprehensively investigated by the IACUC. The final plan is attached.
Related to Protocols: ISMMS GCO numbers 17-0288 (NIH AG057440-01) 14-0141(R01 AG048923-01), and 13-1681-00001-01-PD (Alzheimer's Association).

PI: Dr. Dongming Cai

Funding Source(s) History: Internal department funding, NIH and Alzheimer's Disease

If you require further information please contact the IACUC Chair, Dr. Giorgio Martinelli @ (b) (6)
(b) (6), giorgio.martinelli@mssm.edu

Best regards,

(b) (6)



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Icahn School of Medicine at Mount Sinai

Institutional Animal Care and Use Committee

One Gustave L. Levy Place, Box 1155
New York, NY 10029
Tel: (212) 241-0153
Fax: (212) 241-5550
Email: IACUC@mssm.edu

February 16, 2018

Axel Wolff, MS, 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

Dear Dr. Wolff:

The Icahn School of Medicine at Mount Sinai (ISMMS) Institutional Animal Care and Use Committee (IACUC), in accordance with Assurance D16-00069 (A3111-01), PHS Policy IV.F.3., and NIH Guide Notice NOT-OD-05-034 submits this report regarding an adverse event involving the death of an NHP (rhesus macaque), USDA # 39872, related to protocol IACUC-2014-0004, entitled, "Behavioral and Magnetic Resonance Imaging Investigation of Memory and Cognition", Principal Investigator, Dr. Paula Croxson. The funding source history for this protocol is NIH/NOA1 R21 NS096936-01A1, and a grant from the Multiple Sclerosis Foundation. This incident was first reported to you on January 11, 2018 via telephone and email by (b) (6)

On December 12, 2017 the IACUC received a Veterinary report that a NHP had died after a technician in Dr. Paula Croxson's laboratory had administered to the NHP the cholinesterase inhibitor neostigmine, as part of the above referenced study. The report indicated that, shortly after administering the drug, the technician noted that the NHP was displaying signs of neurological distress and cardio-respiratory depression. The technician immediately sought assistance from (b) (6) (at the time of the incident Dr. Croxson was out of town and her colleague, (b) (6) was in charge of the laboratory.) (b) (6) immediately placed an emergency call for help to the Veterinarians of the Center for Comparative Medicine and Surgery (CCMS). The CCMS Veterinarian, (b) (6) arrived on the scene and noted that the laboratory staff had already initiated CPR. (b) (6) and Veterinary Medicine personnel attempted lifesaving procedures for nearly 90 minutes but were unable to save the NHP. The animal body was sent for a pathological analysis to the CCMS pathology laboratory led by (b) (6). The pathology report, submitted on Dec 14th, 2017 noted that the presence of severe, acute pulmonary edema in

the NHP was a reported effect of an overdose of neostigmine.

The IACUC discussed the incident at a convened emergency meeting on December 21, 2017 and requested that the PI provide a plan for establishing standard operating procedures for avoiding future occurrences of such events.

In a written communication to the IACUC Dr. Croxson agreed with the pathology report that it is likely that the animal received an accidental overdose of neostigmine, likely due to a calculation error in the preparation of the drug. Dr. Croxson expressed deep regret for the loss of a precious animal and provided a firm assurance that, going forward, she and her research personnel would always consult with CCMS Veterinarians regarding drug doses and preparations prior to administering them to the NHPs involved in the study.

After considering all the documentation of the incident and the response of the PI, the IACUC determined that the loss of the NHP was an unfortunate isolated event and not a programmatic failure.

The Icahn School of Medicine at Mount Sinai IACUC is committed to protecting the welfare of animals used in research and appreciates the continued guidance and assistance provided by OLAW in this regard. Should you have any questions regarding this report, please feel free to contact me at

Thank you for your consideration of this matter.

Sincerely,

Eric Nestler, M.D., Ph.D.
Dean for Academic and Scientific Affairs
Director, Friedman Brain Institute
Icahn Building Floor 10 (b) (4)
1425 Madison Avenue
New York, NY 10029
eric.nestler@mssm.edu
(b) (6)

Wolff, Axel (NIH/OD) [E]

From: Wolff, Axel (NIH/OD) [E]
Sent: Tuesday, February 20, 2018 7:18 AM
To: 'Nestler, Eric'
Subject: RE: FINAL report to OLAW RE: CROXSON NHP

Thank you for this report, Dr. Nestler. We will send a response soon.
Axel Wolff

From: Nestler, Eric [mailto:eric.nestler@mssm.edu]
Sent: Friday, February 16, 2018 3:48 PM
To: Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>
Cc: Martinelli, Giorgio <giorgio.martinelli@mssm.edu>
Subject: FINAL report to OLAW RE: CROXSON NHP

Dr. Wolff,

Attached is our final report. Please let us know if you need more.

Thank you,

Eric Nestler

Eric J. Nestler, M.D., Ph.D.
Nash Family Professor of Neuroscience
Director, Friedman Brain Institute
Dean for Academic and Scientific Affairs
Icahn School of Medicine at Mount Sinai
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eric.nestler@mssm.edu

Wolff, Axel (NIH/OD) [E]

A3111-G

From: Wolff, Axel (NIH/OD) [E]
Sent: Thursday, January 11, 2018 2:02 PM
To: (b) (6)
Subject: RE: Preliminary report of two reportable situations

Thank you for this preliminary report and your call, (b) (6) I will start a new case file and look forward to receiving the final report from the IO after the IACUC has completed its investigation.

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

From: (b) (6)@mssm.edu]
Sent: Thursday, January 11, 2018 12:49 PM
To: Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>
Cc: Martinelli, Giorgio <giorgio.martinelli@mssm.edu>
Subject: Preliminary report of two reportable situations
Importance: High

To: Dr. Axel V. Wolff, MS, D.V.M, Director of OLAW

Dear Dr. Wolff,

Per our phone conversation today, on behalf of the Icahn School of Medicine at Mount Sinai IACUC, this email serves as a preliminary report of two reportable incidents occurring at the Institution. Per your recommendation, I have listed the species of the NHP and the funding sources for both Principal Investigators' protocols:

- 1) **Adverse Event involving an NHP:** NHP (rhesus macaque) death, USDA#39872 related to IACUC protocol IACUC-2014-0004
PI: Dr. Paula Croxson
Funding Source(s) History: NIH/NOA 1 R21 NS096936-01A1, and Multiple Sclerosis Foundation
- 2) **Unauthorized transport of animals:** Noncompliance issue related to unauthorized importation of mice. No harm came to the mice. This incident has been comprehensively investigated by the IACUC. The IACUC is in the processes of filing a final report to the I.O. The IACUC is recommending to the IO remedial actions but does not have a final plan yet.
Related to Protocols: ISMMS GCO numbers 17-0288 (NIH AG057440-01) 14-0141(R01 AG048923-01), and 13-1681-00001-01-PD (Alzheimer's Association).
PI: Dr. Dongming Cai
Funding Source(s) History: Internal department funding, NIH and Alzheimer's Disease

A full final report to OLAW will follow before the end of the month.

If you require further information please contact the IACUC Chair, Dr. Giorgio Martinelli @ (b) (6)
(b) (6) giorgio.martinelli@mssm.edu

Best regards,

(b) (6)



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