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

October 11, 2018

Re: Animal Welfare Assurance
#A3290-01 (OLAW Case 1R)

Dr. Todd Evans
Associate Dean for Research
Weill Cornell Medical College
1300 York Avenue, LC710
New York, NY 10065

Dear Dr. Evans,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your October 8, 2018 response to my September 17, 2018 request for additional information on several instances of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Weill Cornell Medical College. According to the information provided, OLAW understands the following:

1) In response to mice being left in an imaging device for three days, the Principal Investigator counseled the laboratory staff, revised the imaging protocol to include a check of the machine and all cages to account for animals, and has each investigator notify the animal technician that the imaging machine is clear.

2) The post-approval monitoring (PAM) for the investigator who failed to provide analgesics and failed to use aseptic technique has not yet been performed. At the next surgery the monitoring will be performed to assess technique.

3) To address the sporadic failure to provide food and water to cages during set up, cages will now be supplied with food and water bottles before being delivered to the animal rooms. When investigators establish new cages, the cages will already be supplied with food and a water bottle. Water bottles have arrows printed on the bottom to show correct orientation. Research and animal care staff share responsibility to ensure that all animal cages have food and water. If animal caretakers miss a cage without food or water, they are retrained and disciplined.

   To address the failure to provide required analgesics, a comprehensive training program is in place for investigators performing surgeries. Training stresses the requirement for providing all analgesics as described in the approved protocol and documenting this. Investigators who fail to give the required analgesics are retrained and may be subject to PAM.

Based on its assessment of these explanations, OLAW has a better understanding of the measures taken to correct and address the noncompliant incidents. We are always available for consultation and have spoken with many institutions about how to address programmatic problems such as repeated incidents of animals dying from lack of food and water. OLAW hereby closes this case but requests an update on incident #4 after the PAM assessment is complete. Thank you for keeping OLAW apprised on these matters.

Sincerely,

(b) (6)

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

cc: IACUC Chair

Weill Cornell Medicine

Institutional Animal Care and Use Committee
1300 York Avenue, Box 5
New York, NY 10065

445 East 69th Street, Olin Hall Rm-423
New York, NY 10065

Telephone: 646-962-2981/2
Email: iacucadmin@med.cornell.edu

October 8, 2018

Re: Assurance # A3290-01 **(OLAW Case 1R)**

Dear Dr. Wolf:

In response to your letter dated September 17, 2018 (OLAW Case 1R) please see the preventive plan developed by the investigator for incident #1, an update on the assessment of the post-approval monitoring and proficiency of the researcher in incident #4 and how the IACUC addressed problems that potentially appear to be programmatic (failure to provide food/water, failure to provide analgesics).

Sincerely,

(b) (6)

Todd R. Evans, Ph.D.
Institutional Official
Associate Dean for Research
Weill Cornell Medicine

1) Provide the preventive plan developed by the investigator for incident #1.

The response from the investigator is as follows:

We have discussed this important issue with all the lab members and have implemented the following measures to prevent such an incident in the future:

1. *In the imaging protocol, we have now included a specific check of the IVIS machine and cages at the end of each imaging session to ensure that all animals are accounted for.*
2. *Furthermore, at the end of the imaging session, each investigator will report to the animal tech via email or text that the IVIS machine is CLEAR.*

2) Provide an update on the assessment of the post-approval monitoring session and proficiency of the researcher in incident # 4.

The PAM session for this investigator has not yet been performed as the surgeon has not scheduled the intracerebral injection surgery. When this surgery is scheduled, the PAM Specialist will observe the surgeon from surgical prep until completion and will report her findings to the IACUC. We can provide a follow-up report at that time.

3) Provide information on how the IACUC addressed problems that potentially appear to be programmatic so that the same issue does not occur in another laboratory. OLAW considers repeat of the same incident (failure to provide food/water, failure to provide analgesics) to constitute a potentially programmatic problem which should be addressed across the animal care and use program.

Failure to provide food and water:

The combined animal care program of MSK and WCM has a daily census of over 60,000 cages. While our goal is to eliminate these types of issues, despite our best efforts these incidents still occur, albeit rarely. As many of these deficiencies result from cages newly set up by the investigative staff we have attempted to eliminate the lack of food and water bottle placement at its root. Food and water bottles are placed within all cages stocked in the animal holding rooms. We have removed access to new cages that do not have both food and water bottles so investigators cannot set up new cages without food and water. This ensures that every cage used by the investigator has food and water properly placed inside when establishing new cages. Additionally, to ensure proper placement of water bottles the bottoms of the bottles have printed white silkscreened arrows indicating the correct orientation.

We view the responsibility to identify that food and water are present as a shared responsibility by the investigative and the animal care staff. Investigators are trained to evaluate their animals on a

regular basis and to determine if food and water is adequate. Investigative staff are trained to be vigilant with water bottle placement as well as food and water levels. All cages are checked daily by the animal care staff and if these cages were not properly identified the staff is retrained and corrective action implemented, up to and including termination.

We have reached out to AAALAC regarding strategies to prevent these type of incidents from occurring and we welcome any suggestions by OLAW.

Failure to provide analgesics:

We have a comprehensive training program for investigators performing surgeries. This includes didactic training and surgical wet labs. All investigators are taught the importance of being aware of the analgesic regimen described in the approved protocol, providing all analgesics and recording the administration of analgesics on the surgery cage card. Failure to provide all analgesics results in retraining of investigators and often a PAM session involving monitoring the surgical procedure by our PAM specialist to be certain that the all analgesics are administered.

Please let us know if any further action is needed on our part.

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September 17, 2018

Re: Animal Welfare Assurance
#A3290-01 (OLAW Case 1R)

Dr. Todd Evans
Associate Dean for Research
Weill Cornell Medical College
1300 York Avenue, LC710
New York, NY 10065

Dear Dr. Evans,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your September 12, 2018 letter reporting seven incidents of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Weill Cornell Medical College. According to the information provided, OLAW understands the following about the incidents and the corresponding corrective actions:

1) Four mice were left in an imaging device for three days.

Corrective action: The mice were treated and recovered. The laboratory staff was counseled and a prevention plan will be developed.

2) Four mice became dehydrated because the cage had no water bottle. The problem was not noted during the daily health check by the animal caretaker.

Corrective action. The mice were treated and recovered. The laboratory staff was counseled and the animal caretaker was retrained.

3) Four mice died and four were dehydrated because the water bottles were incorrectly placed on the cages and water could not be accessed. The laboratory staff was responsible for providing husbandry. The problem was not noted during the daily health check by the animal care staff.

Corrective action: The animal care staff was counseled on checking cages cared for by research staff. The laboratory staff was counseled to ensure that all animals are healthy and have access to food and water.

4) A rat failed to receive the required analgesics following an intracerebral injection and aseptic technique was not used.

Corrective action: The laboratory staff was counseled on using aseptic technique and providing required analgesics. The individual responsible was retrained and will be monitored for proficiency.

5) An adult mouse was subjected to a tail snip without anesthesia or analgesia, contrary to what was required in the approved protocol.

Corrective action: The laboratory staff was counseled on adhering to the protocol and not conducting tail snips on older mice.

6) Mice were housed in a laboratory not approved as a satellite facility. There were no problems with the mice or cages.

Corrective action: The mice were returned to the vivarium and the investigator was directed not to house mice in the laboratory.

7) Several mice failed to receive the required analgesics following cranial surgery. The surgeon was not in the laboratory on the day following surgery and failed to identify an individual to provide the drugs.

Corrective action: All surgeons in the laboratory were counseled on the requirement for providing analgesics as stated in the protocol and on ensuring back up care.

Based on its assessment of these explanations, OLAW understands that measures have been implemented in all situations to correct and prevent recurrence of the problems. While OLAW concurs with the actions taken by the institution to comply with the PHS Policy, please provide the following additional information for completeness of the record:

1) Provide the preventive plan developed by the investigator for incident #1.

2) Provide an update on the assessment of the post-approval monitoring and proficiency of the researcher in incident #4.

3) Provide information on how the Institutional Animal Care and Use Committee addresses problems that potentially appear to be programmatic so that the same issue does not occur in another laboratory. OLAW considers repeat of the same incident (failure to provide food/water, failure to provide analgesics) to constitute a potentially programmatic problem which should be addressed across the animal care and use program.

Please provide the requested information by **October 15, 2018**.

Sincerely,

(b) (6)

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

cc: IACUC Chair

A3290-1R

Weill Cornell Medicine

Institutional Animal Care and Use Committee
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445 East 69th Street, Olin Hall Rm-423
New York, NY 10065

September 12, 2018

Brent Morse, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

Re: Assurance # D16-00186

Dear Dr. Morse:

We are writing to report incidents of non-compliance that occurred within the animal care and use program at Weill Cornell Medicine. The incidents were presented to and discussed by the IACUC during the months of July and August. The incidents and resolutions are as follows:

Incident #1
Four mice were left in an imaging device for 3 days. The mice were dehydrated but recovered with supportive care.
Resolution
The PI was asked to address this issue with his laboratory members and to develop a plan for the laboratory to prevent a recurrence. (United States Department of Defense W81XWH-16-1-0615 & National Cancer Institute 1 F31 CA217032-01)

Incident #2
A cage of four mice was found with no water bottle resulting in animals which were dehydrated. All four mice recovered with supportive care.
Resolution
All cages are checked at least daily by the animal care staff and all stock cages maintained in the room include feed and water. Since this cage was missed during daily animal care staff health checks, the animal care technician assigned to this rooms was retrained and corrective action implemented. The PI was also contacted and asked to address this issue with his lab members and remind them that they should ensure their cages are provided feed and water when being established and are monitored to be ensure the animals are healthy and have adequate food and water.

Incident #3

Four cages of mice were found with water bottles that were placed incorrectly so that mice were not able to access water. Four mice were found dehydrated and four mice were found dead. The cages were identified as "Do Not Disturb (DND)" cages and thus, the animal user is responsible for performing all cage changes utilizing supplies that are in the room (cages and water bottles are separate). The animal user placed the water bottles in the cages incorrectly during the cage change. The animal care staff failed to identify the misplaced bottles when daily health checks were conducted.

Resolution

The staff received counseling/retraining about their responsibilities for checking DND cages and recognition of misplaced water bottles. The PI was also contacted and asked to address this issue with his lab members and to remind them that they should ensure their cages are monitored to confirm the animals are healthy and have adequate food and water.

Incident #4

An investigator performed an intracerebral injection on a rat and the required analgesics, bupivacaine and buprenorphine, were not administered as described in the approved animal protocol nor were appropriate procedures for ensuring aseptic technique used.

Resolution

The PI addressed all lab members performing surgeries about the importance of utilizing aseptic technique and providing all analgesics described in the protocol. The IACUC required that the animal user repeat surgical training and not perform this procedure until the procedure is monitored by a PAM specialist. (These experiments are not PHS funded.)

Incident #5

An adult mouse underwent a tail biopsy procedure without anesthesia or analgesia. The protocol stipulates that only mice up to 17 days old may undergo tail biopsies without anesthesia or analgesia.

Resolution

The PI addressed the issue with all lab members performing tail biopsies and stressed the importance of adhering to the approved protocol and not performing tail biopsies on mice older than 17 days. (National Institute of Diabetes & Digestive & Kidney Diseases 1 R01 DK113088-01A1)

Incident #6

An investigator was found to be housing mice in his laboratory. The approved protocol only allows for mice to be in the laboratory for up to 12 hours. All mice were healthy and all cages were clean.

Resolution

Animal were returned to the vivarium and the investigator agreed not to house animals in the laboratory. (These experiments are not PHS funded.)

Incident #7

Mice underwent a cranial window implant surgery. Post-operative analgesics were not given. The protocol stipulated that carprofen and/or buprenorphine should have been given for up to 48 hours. The surgeon was absent on the day after the surgery and did not designate another lab member to provide the analgesics.

Resolution

The PI addressed all of the surgeons in his laboratory about the importance of providing and recording the administration of all post-operative analgesics described in the approved IACUC protocol and ensuring post-operative care is provided in case the responsible animal user is absent.

(National Institute of Neurological Disorders & Stroke 1 R01 NS100447-01 & 2 R01 NS037853-20)

We believe that these issues have been adequately addressed and that the procedures implemented should prevent recurrence. Should you have any questions or concerns, please contact me at [redacted] or the IACUC Chairman, Dr. Andrew Nicholson, at [redacted] (b) (6).

Sincerely,

[redacted] (b) (6)

Todd R. Evans, Ph.D.
Institutional Official
Associate Dean for Research
Weill Cornell Medicine

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, September 13, 2018 11:51 AM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: Andrew C. Nicholson; Todd R. Evans
Subject: RE: WCM IACUC Incident Report (#D16-00186)

Thank you for this report. We will send 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

From: (b) (6)
Sent: Thursday, September 13, 2018 10:31 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Andrew C. Nicholson <nicholso@med.cornell.edu>; Todd R. Evans <tre2003@med.cornell.edu>
Subject: WCM IACUC Incident Report (#D16-00186)

Dear OLAW:

Please find a WCM IACUC incident report attached and let me know if any further clarifications are required.

Best regards,
(b) (6)

(b) (6)

Weill Cornell Medicine