



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive - MSC 7982
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
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

August 2, 2017

Re: Animal Welfare Assurance
A3177-01 [OLAW Case 1H]

Dr. Martha P. Farrell
General Counsel and
Vice President of Human Resources
Schepens Eye Research Institute
243 Charles Street, (b) (4)
Boston, MA 02114

Dear Dr. Farrell,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your letter dated July 28, 2017 provided in response to our request to provide a specific plan describing program-wide actions and a schedule for implementation to prevent use of expired substances in animals. This request was made after review of your May 11, 2017 letters reporting the use of expired agents and OLAW's concern that these noncompliance incidents indicated a programmatic issue.

Your response outlined the following information. Previous actions to address expired drugs included requiring each lab to designate one responsible individual to manage an inventory system and discard expired items; increased frequency of laboratory inspections; a mandatory training session for all animal users on the importance of not using expired drugs; and presentations given at Faculty, Fellows, and Tech Staff meetings. It was indicated that these previous actions were beneficial, but the likely cause of the recent expired substance incidents were attributed to laboratory staff and research fellow turnover. To address the repeat noncompliance incidents, increased efforts to remind researchers throughout the year were described. The presentations given at Faculty, Fellows, and Tech Staff will now be conducted semi-annually beginning in September 2017, the mandatory training session will now occur annually beginning this fall, and the IACUC has developed a policy regarding the use of expired drugs and repercussions for noncompliance with the policy. The letter indicated that the policy will be implemented after approval which is anticipated on August 3, 2017.

OLAW is satisfied that appropriate actions have been taken to address these incidents of noncompliance on a programmatic level, and that the additional program-wide actions will remind and educate the individuals involved in animal use to reduce the likelihood of recurrence of administration of expired substances to animals. Please contact our office if the corrective programmatic actions are not carried out as described. OLAW appreciates your dedication to your institution's animal care and use program and commitment to compliance with the PHS Policy for the humane care and use of animals. We find no cause for further action at this time.

Sincerely,

(b) (6)

Jane Na, DVM
Veterinary Medical Officer, OLAW
Division of Compliance Oversight

cc: IACUC Contact



**Schepens Eye
Research Institute
Massachusetts Eye and Ear**

July 28, 2017

Jane Na, DVM
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
Bethesda, MD 20892-7982.

Dear Dr. Na,

On May 23, 2017, Schepens Eye Research Institute (#D16-00112) received a response from your office in regards to a letter we submitted on May 11, 2017 reporting the use of expired drugs.

The response from OLAW stated, "We request an update that includes a specific plan describing program-wide actions and a schedule for implementation to prevent use of expired substances. Please provide this information to my attention no later than July 31, 2017."

The IACUC met at a convened meeting on June 1, 2017, with the Institutional Official present, to discuss the ongoing issue of the use of expired drugs in animals. The Committee discussed the previous actions implemented by the IACUC, including (i) the requirement that labs develop an inventory system and assign one specific individual to oversee the inventory and discard all expired pharmaceuticals, (ii) increased lab inspections from semi-annually to quarterly, (iii) holding a mandatory training session for all animal users where the IACUC Chair and Attending Veterinarian presented on the importance of not using expired drugs in animals, and (iv) presentations made at Faculty, Fellows, and Tech Staff meetings. While these actions had an immediate impact, the IACUC believes the recent incidents are likely a result of the turnover in the laboratory staff and research fellows and that multiple reminders/presentations regarding the use of expired drugs must be made throughout the year for all faculty, staff, and fellows.

The IACUC unanimously voted for the implementation of the following program-wide actions in an effort to prevent the use of expired drugs in animals.

1. Semi-annual presentations on the importance of not using expired drugs in animals will be made at faculty meetings (to be presented by the IACUC Chair) and at the fellows and technical staff meetings (to be presented by the Senior IACUC Administrator). These Semi-annual presentations will begin in September 2017.
2. An Annual Institutional wide mandatory training session for all animal users on the importance of not using expired drugs in animals (to be presented by the IACUC Chair and Attending Veterinarian). This annual training session will take place in the Fall of 2017.
3. The IACUC will develop a policy regarding the use of expired drugs and the repercussions that will occur when there is non-compliance with this policy. This policy will (i) explain the regulations regarding the use of expired substances in animals, (ii) provide general guidelines for proper drug storage and disposal, and (iii) outline the repercussions that will occur when there is non-compliance with this policy. Most notably, a second offence will now result in drugs being removed from the laboratory and stored in the Animal Facility pharmacy for a



Harvard Medical School Affiliate

period of time determined by the IACUC. In order to administer any of the stored drugs, investigators must schedule a time to collect the pharmaceuticals needed with a member of the Veterinary staff. In addition researchers must document removal and return of the drug(s) with a member of the Veterinary Staff present. This policy was reviewed in the July IACUC meeting and is currently under revision. The new policy will be implemented immediately following approval in the upcoming August 3rd IACUC meeting.

The IACUC feels strongly that taking these new program-wide actions will prevent future use of expired drugs in live animals.

If you have any further comments or questions, please contact me at Martha_farrell@meei.harvard.edu or by phone at (b) (6)

Sincerely,

(b) (6)

Martha Pyle Farrell
General Counsel & Vice President of Human Resources
Institutional Official

cc: Meredith Gregory-Ksander, Ph.D., IACUC Chair
Patricia D'Amore, Ph.D., Director of Research and Animal Facility Director
Marie Ortega, BA, CPIA, RLATG, Animal Facility Associate Director
AAALAC

Na, Jane (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Monday, July 31, 2017 8:52 AM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: Farrell, Martha Pyle; (b) (6) D'Amore, Patricia; Ortega, Marie
Subject: RE: Schepens Response to OLAW Letter of Non-Compliance (Expired Drugs) D16-00112

Dear (b) (6)

Thank you for the follow-up letter. I will send an official response soon.

Jane

Jane Na, DVM
 Veterinary Medical Officer
 Office of Laboratory Animal Welfare, NIH
 RKL1, Suite 360G
 6705 Rockledge Drive
 Bethesda, Maryland 20892
 Phone (301) 402-1922
 E-fax (301) 451-5609

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From: (b) (6)
Sent: Friday, July 28, 2017 4:49 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Farrell, Martha Pyle <Martha_Farrell@MEEI.HARVARD.EDU> (b) (6)
 (b) (6) D'Amore, Patricia <patricia_damore@meei.harvard.edu>; Ortega, Marie
 <Marie_Ortega@MEEI.HARVARD.EDU>
Subject: Schepens Response to OLAW Letter of Non-Compliance (Expired Drugs) D16-00112

Good Afternoon,

This email is intended for Dr. Jane Na.

Attached please find the letter that the Schepens Eye Research Institute (D16-00112) received from Dr. Jane Na on May 23, 2017 regarding non-compliance for the use of expired drugs. Also attached is our response regarding the issue of the use of expired drugs.

Please do not hesitate to contact me regarding any questions or concerns.

Best,

(b) (6)

Schepens Eye Research Institute/Massachusetts Eye and Ear
 20 Staniford Street
 Boston, MA 02114



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May 23, 2017

Re: Animal Welfare Assurance
A3177-01 [OLAW Case 1H]

Dr. Martha P. Farrell
General Counsel and
Vice President of Human Resources
Schepens Eye Research Institute
243 Charles Street, (b) (4)
Boston, MA 02114

Dear Dr. Farrell,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your letter dated May 11, 2017 regarding noncompliance with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals at the Schepens Eye Research Institute. According to the information supplied, OLAW understands that during a semiannual laboratory inspection, it was noted that an expired bottle of mixed ketamine/xylazine was used to anesthetize mice on March 3, 2017 which was three days past the expiration date (February 29, 2017). The involved animal activity was not PHS supported.

Corrective actions consisted of the Veterinary Technologist removing the expired bottle during the inspection and counseling the laboratory members on the importance of not using expired drugs. The laboratory indicated that they would implement multiple layers of checks to ensure agents are not used after their expiration dates. The changes that were described included that all individuals would set email reminders with expiration dates on their calendars and use a shared internal Excel spreadsheet including drug expirations and brightly colored expiration date labels.

OLAW concurs with the described actions taken to prevent future use of expired drugs but remains concerned due to the repeat nature of this noncompliance. A separate letter, also dated May 11, 2017, was submitted by your institution that described a similar finding of a laboratory that administered expired analgesics to mice on multiple occasions. These findings are suggestive of a programmatic issue that must be further addressed to prevent future situations in which expired substances are administered to animals.

We request an update that includes a specific plan describing program-wide actions and a schedule for implementation to prevent use of expired substances. Please provide this information to my attention no later than **July 31, 2017**. Feel free to contact me should you have any questions.

Sincerely,

(b) (6)

Jane Na, DVM
Veterinary Medical Officer, OLAW
Division of Compliance Oversight

cc: IACUC Contact



**Schepens Eye
Research Institute
Massachusetts Eye and Ear**

A3177-1H

May 11, 2017

Axel V. Wolff, M.S., D.V.M.
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
Bethesda, MD 20892-7982.

Dear Dr. Wolff,

On May 2, 2017, a quorum of the Schepens Institutional Animal Care and Use Committee (IACUC) found, by a unanimous vote, that a laboratory conducted a reportable violation of our Institute's PHS Assurance #D16-00112 and established Schepens IACUC Policies.

The Committee noted that the following violation occurred:

- **Use of expired anesthesia:** During the semi-annual laboratory walk through, the Veterinary Technologist noted that 1 bottle of Ketamine/Xylazine was used on mice 3 days past the expiration date. The anesthetic mix expired on February 29, 2017 and was used on March 3, 2017. The work on this protocol is not NIH-funded. According to animal welfare regulations and NIH guidelines, the use of expired pharmaceuticals, biologics, and supplies is not consistent with acceptable veterinary practice or adequate veterinary care. All expired drugs, including anesthetics and analgesics, must be discarded on or before their date of expiration.

Upon discovery of the violation, the following steps were taken:

- The Veterinary Technologist removed the bottle from the laboratory at the time of the inspection. The Veterinary Technologist also discussed the importance of not using expired drugs with the responsible laboratory members, who acknowledged their mistake.
- The PI responded that under the previous system, one person was responsible for oversight of the controlled drugs. Unfortunately, when this person left the laboratory there was not a smooth transition to another person to pick up the responsibility. The lab will now have every person in the laboratory set email reminders with expiration dates in their individual calendars (in the event that one person leaves) and the lab has also generated a shared internal Excel spreadsheet to log the dose and date of injections that correspond to each vial of Ketamine/Xylazine. In addition, brightly colored labels with expiration dates will be added to the secondary containers to serve as an additional reminder of the expiration date. Together, there will now be multiple layers of checks to ensure the expiration date of pharmaceuticals and biologics is not missed in the future.
- The Committee reviewed the issue of non-compliance at a convened meeting:
 - The committee was informed of the PI's response to the IACUC Chair and the Committee unanimously voted that no further action is required.



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If you have any further comments or questions, please contact me at Martha_farrell@meei.harvard.edu or by phone at (b) (6)

Sincerely,

(b) (6)

Martha Pyle Farrell
General Counsel & Vice President of Human Resources
Institutional Official

cc: Meredith Gregory-Ksander, Ph.D., IACUC Chair
Patricia D'Amore, Ph.D., Director of Research and Animal Facility Director
Marie Ortega, BA, CPIA, RLATG, Animal Facility Associate Director
AAALAC

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, May 16, 2017 3:33 PM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: Martha Pyle Farrell; (b) (6) Patricia D'Amore; Marie Ortega
Subject: RE: Schepens Eye Research Institute (D16-00112) Report of Non-Compliance (Case II)

Thank you for this report (b) (6) We will send an official response soon.

Regards, Brent Morse

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

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From: (b) (6)
Sent: Tuesday, May 16, 2017 2:43 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Martha Pyle Farrell <martha_farrell@meei.harvard.edu>; (b) (6)
(b) (6) Patricia D'Amore <patricia_damore@meei.harvard.edu>; Marie Ortega <Marie_Ortega@MEEI.HARVARD.EDU>
Subject: Schepens Eye Research Institute (D16-00112) Report of Non-Compliance (Case II)

Dr. Wolff,

Attached please find a letter from our Institutional Official, Martha Pyle Farrell, reporting an issue of non-compliance (Case II) that occurred at Schepens Eye Research Institute (Assurance Number: D16-00112).

This occurred in mice on a non NIH funded protocol.

Please feel free to contact me should you have any questions or require additional information.

Thanks,

(b) (6)