From:

Wolff, Axel (NIH/OD) [E]

Sent:

Thursday, February 13, 2020 6:50 AM

To:

Chapman, Deborah L

Subject:

OLAW report

Hello Dr. Chapman,

Please submit a response regarding the actions being taken to address prevention of rodent deaths due to lack of food/water at the University of Pittsburgh. We have received another report of deaths due to lack of water on January 14, 2020. If your IACUC has not fully developed plan, then just send an interim one.

Thank you.

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

To:

Walker, Keri (NIH/OD) [C]

Subject:

A3187-8Q

Case A3187-8Q, University of Pittsburgh

Dear Mr. Huber,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your January 29, 2020 response to my December 9, 2019 request for information on measures being taken to prevent rodent deaths due to lack of food/water at the University of Pittsburgh. According to the information provided, OLAW understands the following:

- The Institutional Animal Care and Use Committee (IACUC) conducted a detailed review of husbandry practices.
- The animal care and use program is committed to preventing animal deaths due to human error.
- A training program is in place for new animal caretakers who are closely supervised until considered proficient.
- Husbandry errors result in retraining.
- Newly weaned rodents are monitored by Division of Laboratory Animal Resources (DLAR) staff to ensure good health and provision of food/water.
- An enhanced DLAR training program has been implemented and a new Training Manager has been hired. The training will include animal care and research staff.
- Two additional training staff have also been hired.

Responses to OLAW's specific questions are as follows:

- A root cause of why the problems occurred was conducted and concluded that incidents of rodent deaths
 occurred in different facilities and involved different staff and supervisors. There were no repeat failures by the
 same staff.
- 2) In addition to retraining, an incentive program has been established which rewards staff that identify mock cages missing food/water.
- Staff performance problems are documented in employee records and repeat violations are addressed by increasing discipline.
- 4) The institution is aware that any animal death due to human error is unacceptable and is committed to achieving 100% compliance.
- 5) The IACUC is involved in the proposed corrective actions and is requiring all animal care staff to enroll in the new training program. The IACUC will monitor improvement in animal husbandry. The IACUC, DLAR, and investigators are invested in continuing improvement. The number of staff should be proportionate to the number of animals.

OLAW received the January 14, 2020 report which stated that one sentinel mouse died and one required treatment due to not having water. The corrective action consisted of retraining the caretaker on the conduct of daily health checks and all animal facility staff was counseled. A letter of reprimand was issued to the Executive Director of the animal care program and their supervisor.

Based on its assessment of the actions being proposed or already in place, OLAW finds them to be an acceptable approach to achieve the goal of significantly reducing or eliminating rodent deaths caused by human error. We are confident that measures such as the mock cages are a positive approach which should yield the expected results because they have been successfully applied at other institutions facing the same problem. As with similar cases, OLAW is obligated to monitor the success of the proposed program and is hereby placing the University of Pittsburgh on an enhanced reporting schedule. Under this schedule OLAW is requesting an update every two months on the first day of

the month to report success as measured by a reduction in deaths. Near misses that have been successfully caught and corrected should also be reported. Any other metrics such as the status of the mock cage program, the percentage of people trained, and any additional hires should be included. Reportable events, including deaths due to lack of food/water are to be independently promptly reported. We look forward to receiving the first report on April 1, 2020. Feel free to contact me should you have any questions.

cc: IACUC Chair

From:

Wolff, Axel (NIH/OD) [E]

Sent:

Tuesday, February 18, 2020 6:52 AM

То:

Chapman, Deborah L

Subject:

RE: OLAW Case A3187-8Q

Hi Dr. Chapman,

Thanks for this information. I will adjust the calendar to ensure that we know when to expect your enhanced reporting file and will have U of Pittsburgh be set for the 15th, every 2 months. Yes, I will personally handle this but the reports should still go to olawdco@od.nih.gov (which Dr. Morse also monitors). Any other questions, just let me know.

Axel Wolff

From: Chapman, Deborah L <dlc7@pitt.edu> Sent: Friday, February 14, 2020 10:25 AM

To: Walker, Keri (NIH/OD) [C] <keri.walker@nih.gov>; Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>

Subject: Re: OLAW Case A3187-8Q

Dear Dr. Wolff,

The DLAR will start collecting the requested data immediately. The IACUC and DLAR leadership group met with the Institutional Official (IO) today. Because data will need to be collated from 9-10 separate facilities, the DLAR asked whether these reports can be submitted by the 15th of the following month, such that so that the Feb-March report would arrive to you by the 15th of April and so on.

Also the IO wanted to make sure these reports were sent to the correct person. These reports should come directly to you, right? Should they also be cc'd to Dr. Morse?

Thank you for your time.

Debbie

Deborah L. Chapman, Ph.D. Associate Professor Department of Biological Sciences

Chair, Institutional Animal Care and Use Committee

University of Pittsburgh 102 Life Sciences Annex Fifth & Ruskin Avenues Pittsburgh, PA 15260

tel (office): (b) (6) fax: (b) (6)

From: "Walker, Keri (NIH/OD) [C]" < keri.walker@nih.gov>

Date: Thursday, February 13, 2020 at 11:16 AM

To: "Huber, George A" <ghuber@pitt.edu>

Cc: Deborah Chapman < dlc7@pitt.edu>

Subject: OLAW Case A3187-8Q

Dear Mr. Huber,

Attached please find Dr. Wolff's interim response to OLAW Case A3187-8Q.

If you have any questions, feel free to contact us by phone or by e-mail.

Best Regards, Keri

Keri Walker
Program Specialist (Contractor)
Office of Laboratory Animal Welfare
National Institutes of Health
6700B Rockledge Dr., Suite 2500
Bethesda, MD 20892
301-435-2390
keri.walker@nih.gov



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:
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
<u>Telephone</u>: (301) 496-7163
<u>Facsimile</u>: (301) 480-3387

February 13, 2020

Re: Animal Welfare Assurance #A3187-01 [OLAW Case 8Q]

Mr. George A. Huber
Vice Chancellor for Research Conduct
and Compliance
University of Pittsburgh

(b) (4) Hieber Building
3500 Fifth Avenue
Pittsburgh, PA 15213

Dear Dr. Huber,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your January 29, 2020 response to my December 9, 2019 request for information on measures being taken to prevent rodent deaths due to lack of food/water at the University of Pittsburgh. According to the information provided, OLAW understands the following:

- The Institutional Animal Care and Use Committee (IACUC) conducted a detailed review of husbandry practices.
- The animal care and use program is committed to preventing animal deaths due to human error.
- A training program is in place for new animal caretakers who are closely supervised until considered proficient.
- Husbandry errors result in retraining.
- Newly weaned rodents are monitored by Division of Laboratory Animal Resources (DLAR) staff to ensure good health and provision of food/water.
- An enhanced DLAR training program has been implemented and a new Training Manager has been hired. The training will include animal care and research staff.
- Two additional training staff have also been hired.

Responses to OLAW's specific questions are as follows:

- A root cause of why the problems occurred was conducted and concluded that incidents of rodent deaths occurred in different facilities and involved different staff and supervisors. There were no repeat failures by the same staff.
- 2) In addition to retraining, an incentive program has been established which rewards staff that identify mock cages missing food/water.

Page 2 – Mr. Huber February 13, 2020 OLAW Case A3187-80

- 3) Staff performance problems are documented in employee records and repeat violations are addressed by increasing discipline.
- 4) The institution is aware that any animal death due to human error is unacceptable and is committed to achieving 100% compliance.
- 5) The IACUC is involved in the proposed corrective actions and is requiring all animal care staff to enroll in the new training program. The IACUC will monitor improvement in animal husbandry. The IACUC, DLAR, and investigators are invested in continuing improvement. The number of staff should be proportionate to the number of animals.

OLAW received the January 14, 2020 report which stated that one sentinel mouse died and one required treatment due to not having water. The corrective action consisted of retraining the caretaker on the conduct of daily health checks and all animal facility staff was counseled. A letter of reprimand was issued to the Executive Director of the animal care program and their supervisor.

Based on its assessment of the actions being proposed or already in place, OLAW finds them to be an acceptable approach to achieve the goal of significantly reducing or eliminating rodent deaths caused by human error. We are confident that measures such as the mock cages are a positive approach which should yield the expected results because they have been successfully applied at other institutions facing the same problem. As with similar cases, OLAW is obligated to monitor the success of the proposed program and is hereby placing the University of Pittsburgh on an enhanced reporting schedule. Under this schedule OLAW is requesting an update every two months on the first day of the month to report success as measured by a reduction in deaths. Near misses that have been successfully caught and corrected should also be reported. Any other metrics such as the status of the mock cage program, the percentage of people trained, and any additional hires should be included. Reportable events, including deaths due to lack of food/water are to be independently promptly reported. We look forward to receiving the first report on April 1, 2020. Feel free to contact me should you have any questions.

Sincerely,

(b) (6)

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

cc: IACUC Chair



George A. Huber, JD, MSIE, MSSM Vice Chancellor for Research Protections Professor of Health Policy and Management

January 29, 2020

Brent Morse, DVM, DACLAM NIH Office of Laboratory Animal Welfare Rockledge One, Suite 360 6705 Rockledge Drive – MSC 7982 Bethesda, MD 20892-7982

RE: OLAW Case 80

Dear Dr. Morse:

We appreciate the opportunity to respond to OLAW's inquiries pursuant to the University of Pittsburgh's November 27, 2019 letter. We are pleased that OLAW acknowledged our efforts to implement measures to maintain compliance with the PHS Policy on Humane Care and Use of Laboratory Animals. In addition to those measures, the IACUC conducted a detailed review of rodent husbandry practices this month.

The University of Pittsburgh's animal care program is significant and while our goals are to be 100% compliant, we request that the contents of the November 27th letter be reviewed in context of our program size and the period of time in question, which was the three (3) month period of April through June of 2019. We have answered your specific questions below, but would like to take this opportunity to reiterate our commitment to animal care and provide you with information about or most recent efforts to achieve our goal of 100% compliance.

Our training programs and procedures are designed to achieve zero animal losses due to errors in husbandry practices. Procedures are in place at multiple levels to mitigate errors. The training program provided by the Division of Laboratory Animal Resources (DLAR) includes hands-on training for new animal care technicians, direct oversight of new technicians prior to allowing them to independently engage in husbandry duties, and verification of successful husbandry task completion by facility supervisors until new employee proficiency is verified. Daily checking for food, water, and animal health is a critical part of this training. In addition, if a husbandry error is detected, the involved technician receives retraining, as does the entire husbandry staff of the facility, during daily meetings.

Additional husbandry oversight is provided by the DLAR staff for newly-weaned animals. Newly weaned boxes of rodents are marked by research personnel for enhanced monitoring by DLAR staff members to ensure that these animals thrive after weaning. This demarcation also serves as a double check to ensure that newly established boxes are provided with food and water.

Office of Research Protections

Suite 401, Hieber Bullding 3500 Fifth Avenue Plttsburgh, PA 15213 412-624-2202 ghuber@pltt.edu orp.pitt.edu Brent Morse, DVM, DACLAM Page 2 January 29, 2020

We have just launched an enhanced DLAR training program (January 2020), for which the DLAR created and filled a new Training Manager position (2019). The Training Manager has been working to develop an enhanced training program for both animal care staff and investigators, which includes the implementation of additional didactic and hands-on training for research personnel and departmental technicians. With two new training staff members hired in January of 2020, this new arm of the DLAR will help the University of Pittsburgh achieve an even better level of training of research personnel and animal care staff members. We believe that additional training of all groups handling animals will help us achieve our goal of zero animal loss due to husbandry errors.

Below are the University's responses to OLAW's questions:

1) Has a root cause analysis been conducted to determine the cause of these repeat deficiencies (i.e. insufficient training, insufficient supervision, insufficient staffing)?

Yes. We evaluated the possibility of a common root cause for these incidents. The University of Pittsburgh's rodent program is spread over 10 facilities. The reported incidents involved different staff members at different facilities, each with different supervisors. These staff members have not repeated husbandry errors, which attests to the success of our retraining of individuals. These staff members have different levels of experience in our animal care and use program, such that errors do not appear to be linked to training of particular employees.

2) While retraining may be an appropriate response to address something such as use of different caging, it is not adequate when negligence results in animals dying due to lack of food/water. All staff should be aware that animals require food/water in order to survive and additional steps must be taken to ensure adequate husbandry.

We agree that basic retraining does not address this issue. That is why we are supplementing our approach by implementing a mock rodent cage program, which demonstrated success in mitigating loss. A mock rodent cage that is missing food and/or a water bottle is randomly placed in racks across the program. The day when the boxes are installed as well as the day when they are discovered by the staff will be recorded. Contests will be held between and within facilities with the facility finding the largest number of mock boxes winning an incentive and any facility that finds over 75% of the mock boxes within two days also receives an incentive. This program is designed to reinforce the amount of time it takes to recognize an issue in a rodent cage. We are confident that this initiative, together with our enhanced training programs, will help us achieve our goals.

3) Repeat instances of failing to provide food/water or failing to adequately monitor animals must be addressed with escalating sanctions for staff and supervisors.

Monitoring of staff performance by the DLAR is consistent with the University's Human Resources policies. All performance incidents are documented in employee records, and there is a progressive discipline process for all staff that is implemented when errors occur following retraining. It is of note that none of the husbandry incidents included in the November 27th letter were associated with one individual staff member, indicating that our retraining program is effective.

Brent Morse, DVM, DACLAM Page 3 January 29, 2020

4) OLAW realizes that seven noncompliant fatal food/water issues over several months may not appear to be of great magnitude in a large program, however such failures constitute a serious animal welfare concern and steps must be taken to prevent them throughout the program. We agree that while the report represented .0002% of the rodent boxes maintained during the three-month period, our target is 0% and we are working very hard to achieve that goal. We have outlined the efforts we have and plan to take to become 100% compliant. We consider all animal loss to be very serious and are confident that our hiring of a training manger and two trainers to implement an enhanced training program, along with initiatives to focus attention to detail, will allow us to achieve our goal of zero animal loss due to husbandry errors.

5) Provide information on how the Institutional Animal Care and Use Committee plans to address the matter program wide to include animal care staff, technicians, laboratory staff, veterinarians, investigators, supervisors, and facility managers.

The IACUC Compliance Office shared the outcomes of an independent investigation of animal husbandry practices with the full IACUC at its monthly meeting on January 27, 2020 and a pathway moving forward to address enhancing staff training. Beginning in February, all animal care staff, regardless of length of employment, will be required to enroll in the new training program referenced above. The IACUC will monitor the program's success in improving animal husbandry at monthly meetings and will recommend changes as necessary. The IACUC emphasized that IACUC, DLAR, and investigators continue to work cohesively to ensure the success of the program. The IACUC also recommended that the University ensure that its staffing numbers maintain proportionate to the size of our animal program.

Sincerely,
(b) (6)
George A. Huber

From:

Wolff, Axel (NIH/OD) [E]

Sent:

Thursday, February 13, 2020 7:17 AM

To:

(b) (6)

Subject:

RE: OLAW report

Thank you for this report,

(b) (6) I will respond soon.

Axel Wolff

From:

(b) (6)

Sent: Thursday, February 13, 2020 7:06 AM

To: Chapman, Deborah L <dlc7@pitt.edu>; Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>; Huber, George A

<ghuber@pitt.edu> Subject: OLAW report

Attached is our email containing the response. Please let us know if you need something more than this. Thank you.

(b) (6)

From: Chapman, Deborah L <dlc7@pitt.edu> Sent: Thursday, February 13, 2020 7:00 AM

To: Wolff, Axel (NIH/OD) [E] < wolffa@od.nih.gov >; Huber, George A < ghuber@pitt.edu >;

Subject: Re: OLAW report

Dear Dr. Wolff,

The full IACUC met on January 27th and our Institutional Official (cc'd here) submitted a response either on the 28th or the 29th. I am also coing his office so that they can send the letter directly to you.

Sorry that the letter did not reach you.

Debbie

Deborah L. Chapman, Ph.D.

Associate Professor

Department of Biological Sciences

Chair, Institutional Animal Care and Use Committee

University of Pittsburgh

102 Life Sciences Annex

Fifth & Ruskin Avenues

Pittsburgh, PA 15260

tel (office):

(b) (6)

fax:

(b) (6)

From: "Wolff, Axel (NIH/OD) [E]" <wolffa@od.nih.gov>

Date: Thursday, February 13, 2020 at 6:50 AM

To: Deborah Chapman < dlc7@pitt.edu>

Subject: OLAW report

Hello Dr. Chapman,

Please submit a response regarding the actions being taken to address prevention of rodent deaths due to lack of food/water at the University of Pittsburgh. We have received another report of deaths due to lack of water on January 14, 2020. If your IACUC has not fully developed plan, then just send an interim one.

Thank you.

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

From: Sent: To: Subject:	Wolff, Axel (NIH/OD) [E] Thursday, February 13, 2020 7:02 AM Chapman, Deborah L RE: OLAW report
Thanks for the quick response, Dr AW	. Chapman. I'll keep a watch out for the report.
From: Chapman, Deborah L <dlc7 (6)="" (b)="" (nih="" 13,="" 2020="" <wol="" [e]="" axel="" february="" od)="" olaw="" re:="" report<="" sent:="" subject:="" td="" thursday,="" to:="" wolff,=""><td></td></dlc7>	
Dear Dr. Wolff, The full IACUC met on January or the 29th. I am also cc'ing his Sorry that the letter did not reach Debbie	27th and our Institutional Official (cc'd here) submitted a response either on the 28th office so that they can send the letter directly to you.
Deborah L. Chapman, Ph.D.	
Associate Professor	
Department of Biological Sciences	s
Chair, Institutional Animal Care a	nd Use Committee
University of Pittsburgh	
102 Life Sciences Annex	
Fifth & Ruskin Avenues	
Pittsburgh, PA 15260	
tel (office): (b) (6) fax: (b) (6)	

From: "Wolff, Axel (NIH/OD) [E]" <wolffa@od.nih.gov>

Date: Thursday, February 13, 2020 at 6:50 AM

To: Deborah Chapman < dlc7@pitt.edu>

Subject: OLAW report

Hello Dr. Chapman,

Please submit a response regarding the actions being taken to address prevention of rodent deaths due to lack of food/water at the University of Pittsburgh. We have received another report of deaths due to lack of water on January 14, 2020. If your IACUC has not fully developed plan, then just send an interim one.

Thank you.

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



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

December 9, 2019

Re: Animal Welfare Assurance #A3187-01 [OLAW Case 8Q]

Mr. George A. Huber
Vice Chancellor for Research Conduct
and Compliance
University of Pittsburgh

(b) (4) Hieber Building
3500 Fifth Avenue
Pittsburgh, PA 15213

Dear Dr. Huber,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your November 27, 2019 letter reporting seven serious deviations from the provisions of the *Guide for the Care and Use of Laboratory Animals* at the University of Pittsburgh. According to the information provided, OLAW understands the following about the incidents and the corresponding corrective actions:

 Two mice died due to lack of water caused by using the wrong cages on an automatic watering rack which prevented the mice from reaching the lixits. Nine pups and one adult survived. The cages had been incorrectly marked, thus leading to the dehydration deaths.

Corrective actions: The surviving mice were given water, diet gel, and were monitored. The animal caretaker was retrained on which mouse cages to use on which racks and the cage wash technician was trained on the various types of mouse cages, how to mark them, and how they are placed on racks.

 Eight mice died due to lack of food. The animals had been weaned and placed into new cages without food and the animal care staff failed to identify the problem during daily health checks.

Corrective actions: The husbandry staff was retrained and monitored. The laboratory's standard operating procedure for weaning was revised to require notification of a supervisor following weaning to verify provision of food/water.

3) Two mice died due to lack of food. Food had not been added following a cage change and the problem was not identified by husbandry staff during daily health checks.

Corrective actions: The caretaker responsible was retrained on cage changing and health checks.

4) Three of five mice died due to lack of food and the problem was not identified during daily health checks.

Corrective actions: The surviving mice were given food and were monitored. The husbandry staff was retrained and observed performing health checks. The investigator modified that food hoppers to accommodate the experimental powdered food.

5) Two mice died of dehydration due to a missing water bottle. A laboratory member had moved the cage to the wrong rack and the problem was not identified during daily health checks.

Corrective actions: The animal caretakers were retrained and new laboratory staff will be counseled on ensuring food/water for all animals.

 A mouse died because it had crawled into the feeder during cage change and could not access the water.

Corrective actions: The animal caretaker was retrained on cage changing, health checks, and was monitored. All staff was counseled on this incident.

7) One dead and one live mouse were found in a cage without food. The mice had been weaned but not given food and the problem was not identified during daily health checks.

Corrective actions: The surviving mouse was given food mush, the animal caretaker for the room was retrained, all facility caretakers were counseled, the laboratory member responsible was retrained on weaning, and the facility manger was counseled.

In each situation, a letter of reprimand was issued to the Attending Veterinarian, the Principal Investigator, and their supervisors.

Based on its assessment of these explanations, OLAW understands that measures have been implemented in each case to address and correct the problem. While OLAW concurs with overall actions taken by the institution to comply with the PHS Policy on Humane Care and Use of Laboratory Animals, the ongoing nature of these husbandry failures is of concern to this Office. Before potentially placing the University of Pittsburgh on an enhanced reporting schedule, please address the following:

- 1) Has a root cause analysis been conducted to determine the cause of these repeat deficiencies (i.e., insufficient training, insufficient supervision, insufficient staffing)?
- 2) While retraining may be an appropriate response to address something such as use of different caging, it is not adequate when negligence results in animals dying due to lack of food/water. All staff should be aware that animals require food/water in order to survive and additional steps must be taken to ensure adequate husbandry.
- 3) Repeat instances of failing to provide food/water or failing to adequately monitor animals must be addressed with escalating sanctions for staff and supervisors.
- 4) OLAW realizes that seven noncompliant fatal food/water issues over several months may not appear to be of great magnitude in a large program, however such failures constitute a serious animal welfare concern and steps must be taken to prevent them throughout the program.
- 5) Provide information on how the Institutional Animal Care and Use Committee plans to address the matter program wide to include animal care staff, technicians, laboratory staff, veterinarians, investigators, supervisors, and facility managers.

Please provide any and all information on the steps being taken to prevent animal deaths due to lack of food/water by **January 6**, **2020**. Upon evaluation of the proposed plan and schedule, this Office will determine which additional steps need to be taken to ensure compliance. Feel free to contact me should you have any questions.

Page 2 – Dr. Huber December 9, 2019 OLAW Case A3187-8Q

Sincerely,

(b) (6)

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

cc: IACUC Chair



George A. Huber, JD, MSIE, MSSM Vice Chancellor for Research Protections Professor of Health Policy and Management

November 27, 2019

Brent Morse, DVM, DACLAM NIH Office of Laboratory Animal Welfare Rockledge One, Suite 360 6705 Rockledge Drive – MSC 7982 Bethesda, MD 20892-7982

Dear Dr. Morse:

As the Institutional Official responsible for the University of Pittsburgh's Animal Care and Use Program (IACUC) (Assurance number D16-00118), I am writing to report several incidents that occurred over the course of the past year in our animal facilities. Notification of the incidents was provided to the IACUC in August and September. They are described below, followed, for the sake of clarity, by the corrective action plan for the incident, as well as whether an involved investigator

receives NIH or NSF funding.

On March 26, 2019, a two mouse boxes in an auto water cage rack were discovered with a collective total of one adult mouse, two deceased adult mice, and nine surviving mouse pups. It was determined that when the cages were changed on March 23 and 24, 2019, although the lixits in both boxes were functioning properly, the technician inserted the incorrect mouse boxes when doing the room change, and the lixit was higher than the adult mice could reach. This error was the result of the cages being mismarked. The surviving mouse pups were provided diet gel and water and monitored. The surviving adult mouse was provided diet gel and water and monitored but died the following day.

o The animal care technician involved was retrained on the proper style of boxes to use for each rack.

The cage wash technician involved was retrained on the different types of mouse cages and how each are to be placed and marked following washing.

On April 14, 2019, two boxes totaling 8 dead mice were found without access to food. The animals had been weaned up to two days earlier, placed in boxes, but not provided with food. Animal care technicians failed to notice the lack of food during their rounds.

The technicians involved in performing daily room checks were retrained, observed performing box checks, and spot checked for several days.

O The investigator will update his lab's standard protocol for weaning to include an email from whomever performed the weaning to a supervisor, who will ensure that each new box has been handled appropriately, including having food provided.

Suite 401, Hieber Building 3500 Fifth Avenue Pittsburgh, PA 15213 412-624-2202 ghuber@pitt.edu orp.pitt.edu o The investigator's research is supported by the following NIH grants: 5R01DK109907-04 BRANCHED CHAIN ACYL-COA METABOLISM AND DISEASE

5R01DK078775-12 INBORN ERRORS OF LONG CHAIN FAT METABOLISM

- On May 12, 2019, a box containing two deceased adult mice were found without access to
 food during morning room checks. The box had been changed on May 6, 2019 and it was
 assumed that no food was added at the time of the box change. The lack of food had been
 missed by several technicians doing daily room checks.
 - The animal care technician involved was retrained on performing box changes and performing daily room checks.
- On May 23, 2019, five mice were found without access to food. Three of the mice were dead.
 Upon discovery, the surviving mice were provided with food by animal care staff and monitored for seventy-two hours.

 The technicians involved in performing daily room checks were retrained, observed performing box checks, and spot checked for several days.

o The investigator has outfitted the in-cage food containers with a cover with small holes in order to allow the mice access to the special powdered food required for the study and prevent food spilwlage if the container is overturned.

The investigator's research is supported by the following NIH grant:

5R01CA174713-05 CONTROL OF METABOLISM AND ENERGYSENSING PATHWAYS BY C-MYC

On June 3, 2019, two adult mice were found dead in their cages and without access to water. The cage was found on a water bottle cage rack but missing a water bottle. It was determined that a member of the investigator's staff moved the box to the wrong rack on May 30, 2019. Animal care technicians did not notice that the water bottle was missing for four days.

 The event and retraining of staff was discussed at a morning meeting of animal facility staff.

- O To avoid any such mishaps in the future, this event will be highlighted to any new laboratory staff being trained to manage animals. The investigator will explain to new staff the need for vigilance and thoroughness in their working with experimental animals.
- The investigator's research is not supported by NIH grants.

On June 14, 2019, a box on an auto water rack containing one deceased adult mouse was
discovered during a routine cage change. It was assumed that the mouse crawled into the
feeder during the last cage change on June 7, 2019. No other mice were affected.

o The technician involved was retrained on performing OptiMice cage changes and ensuring the food hopper is full to prevent mice from climbing into the hopper during cage changes. The technician was observed performing cage changes and retrained on daily box checks.

 The event and preventative actions were discussed with all personnel during a morning meeting.

- On June 27, 2019, a box containing two recently weaned mouse was found without access
 to food. One of the pups was dead. Upon discovery, animal care staff provided mush to
 the surviving pup daily for two days. The animals had been weaned by the investigator's
 staff two days earlier, placed in boxes, but not provided with food. DLAR technicians
 did not notice the lack of food in the box for two days.
 - o The technician performing daily room checks was retrained.
 - The situation was reviewed and discussed with all facility animal care technicians.
 - o To prevent this from occurring again, the investigator reviewed the staff members' process for weaning, including double checking each box for food before it is put on the rack.
 - Additionally, the investigator discussed the situation with the facility manager who oversees the holding room.

The University of Pittsburgh IACUC reviewed and accepted the investigator's corrective action plan (CAP), which are described after each item above.

For each incident, the IACUC has levied the following sanctions:

1. A letter of reprimand was sent to the Attending Veterinarian, to each Principal Investigator, and their supervisors regarding these violations. The letters have been placed in our files as evidence of a violation.

Please do not hesitate to contact me if you have any questions or concerns.

Sincerely,	(b) (6)
George A. Huber	

From:

Wolff, Axel (NIH/OD) [E]

Sent:

Thursday, December 12, 2019 6:48 AM

To:

Chapman, Deborah L

Subject:

RE: Initial response for A3187-8Q

Yes, Dr. Chapman, we can certainly extend the response deadline to allow your committee to develop a thorough response to a serious issue. I will place your request in the case file and look forward to receiving a final or interim report before the end of January.

Axel Wolff

From: Chapman, Deborah L <dlc7@pitt.edu>
Sent: Wednesday, December 11, 2019 3:16 PM
To: Wolff, Axel (NIH/OD) [E] <wolffa@od.nih.gov>
Subject: FW: Initial response for A3187-8Q

Hello Dr. Wolff,

We received your letter regarding OLAW case 8Q (attached) on Monday only after our Dec. full IACUC meeting had ended. This letter requires at least one response requiring input from the full IACUC committee. Your letter requests a response by January 6, 2020. Is it possible to extend that deadline until after the next full committee meeting, which is scheduled for Jan. 27, 2020? Please let me know if you would like to discuss this further.

Sincerely, Debbie

Deborah L. Chapman, Ph.D. Associate Professor Department of Biological Sciences

Chair, Institutional Animal Care and Use Committee

University of Pittsburgh 102 Life Sciences Annex Fifth & Ruskin Avenues Pittsburgh, PA 15260

tel (office):

(b) (6)

From: "Ward, Joan (NIH/OD) [E]" < wardjoa@od.nih.gov >

Date: Monday, December 9, 2019 at 2:19 PM

To:

(b) (6)

Cc: Deborah Chapman < dlc7@pitt.edu>
Subject: Initial response for A3187-8Q

Dear Dr. Huber,

Attached please find Dr. Axel Wolff's initial response to OLAW Cases A3187-8Q.

If you have any questions, feel free to contact us by phone or by e-mail.

Best Regards,

Joan

Joan Ward Program Specialist Office of Laboratory Animal Welfare National Institutes of Health 6700B Rockledge Dr., Suite 2500 Bethesda, MD 20892 301-496-7163 wardjoa@od.nih.gov

From:

Chapman, Deborah L <dlc7@pitt.edu>

Sent:

Thursday, December 12, 2019 8:54 AM

To:

Wolff, Axel (NIH/OD) [E]

Subject:

Re: Initial response for A3187-8Q

Thank you! I don't want to rush responses and not have the full committee's opinions! Debbie

--

Deborah L. Chapman, Ph.D. Associate Professor Department of Biological Sciences

Chair, Institutional Animal Care and Use Committee

University of Pittsburgh 102 Life Sciences Annex Fifth & Ruskin Avenues Pittsburgh, PA 15260

tel (office):

(b) (6)

From: "Wolff, Axel (NIH/OD) [E]" <wolffa@od.nih.gov>

Date: Thursday, December 12, 2019 at 6:47 AM

To: Deborah Chapman < dlc7@pitt.edu > Subject: RE: Initial response for A3187-8Q

Yes, Dr. Chapman, we can certainly extend the response deadline to allow your committee to develop a thorough response to a serious issue. I will place your request in the case file and look forward to receiving a final or interim report before the end of January.

Axel Wolff

From: Chapman, Deborah L <<u>dlc7@pitt.edu</u>>
Sent: Wednesday, December 11, 2019 3:16 PM
To: Wolff, Axel (NIH/OD) [E] <<u>wolffa@od.nih.gov</u>>
Subject: FW: Initial response for A3187-8Q

Hello Dr. Wolff,

We received your letter regarding OLAW case 8Q (attached) on Monday only after our Dec. full IACUC meeting had ended. This letter requires at least one response requiring input from the full IACUC committee. Your letter requests a response by January 6, 2020. Is it possible to extend that deadline until after the next full committee meeting, which is scheduled for Jan. 27, 2020? Please let me know if you would like to discuss this further.

Sincerely, Debbie

Deborah L. Chapman, Ph.D. Associate Professor Department of Biological Sciences

Chair, Institutional Animal Care and Use Committee

University of Pittsburgh 102 Life Sciences Annex Fifth & Ruskin Avenues Pittsburgh, PA 15260

tel (office):

(b) (6)

From: "Ward, Joan (NIH/OD) [E]" <wardjoa@od.nih.gov>

Date: Monday, December 9, 2019 at 2:19 PM

To:

(b) (6)

Cc: Deborah Chapman < dlc7@pitt.edu > Subject: Initial response for A3187-8Q

Dear Dr. Huber,

Attached please find Dr. Axel Wolff's initial response to OLAW Cases A3187-8Q.

If you have any questions, feel free to contact us by phone or by e-mail.

Best Regards, Joan

Joan Ward Program Specialist Office of Laboratory Animal Welfare National Institutes of Health 6700B Rockledge Dr., Suite 2500 Bethesda, MD 20892 301-496-7163 wardjoa@od.nih.gov

Morse, Brent (NIH/OD) [E]

From:

OLAW Division of Compliance Oversight (NIH/OD)

Sent:

Wednesday, November 27, 2019 1:25 PM

To:

(b) (6) OLAW Division of Compliance Oversight (NIH/OD)

Subject:

RE: University of Pittsburgh

Thank you for providing these reports

(b) (6) We will send official responses soon.

Best regards, Brent Morse

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

Please note that this message and any of its attachments are intended for the named recipient(s) only and may contain confidential, protected or privileged information that should not be distributed to unauthorized individuals. If you have received this message in error, please contact the sender.

From:

(b) (6

Sent: Wednesday, November 27, 2019 12:58 PM

To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>

Subject: University of Pittsburgh

Please review the attached correspondence forwarded on behalf of George A. Huber, Vice Chancellor for Research Protections. Thank you.

(b) (6)