



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 10, 2018

Re: Animal Welfare Assurance  
A4683-01 [OLAW Case B]

Dr. Steve Street  
Vice President, General Manager and  
Head Early Development  
Covance Laboratories, Inc.-Greenfield  
3301 Kinsman Boulevard  
Madison, WI 53704

Dear Dr. Street,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your October 1, 2018 letter reporting two serious deviations from the provisions of the *Guide for the Care and Use of Laboratory Animals* at Covance Laboratories, Inc., following up on an initial report on September 18, 2018. According to the information provided, OLAW understands the following about the incidents and the corresponding corrective actions:

- 1) A rat dam and 11 pups were found to be without a feeder and two pups had died. The animals were thin and unthrifty. The problem was not identified during several daily health checks and it is possible that the feeder was removed for visualization and was not returned.

Corrective action: The mother and litter were euthanized.

- 2) Nineteen rats were found without feeders. The animals were in good condition.

Corrective action: The rats were given food and subsequently removed from study eligibility and euthanized.

Current procedures are in place to ensure that all animals have access to food, staff is adequately trained, health checks are conducted twice daily, and disciplinary policies are in place to address noncompliance. Following these two incidents the following corrective actions have been implemented:

- 1) If a feeder is removed to access animals, it should be hung on the front of the cage to alert staff, and then returned to the inside of the cage. Staff has been trained on this procedure.
- 2) The technicians involved in the incidents have been retrained on the conduct of health checks.
- 3) Health check data will be reviewed by managers to ensure completion of tasks.
- 4) Signs have been posted in animal rooms to remind staff to check for food and water during health checks.
- 5) Any individuals who fail to complete health checks correctly will be disciplined.

- 6) Ongoing meetings will be held with senior animal care program officials and husbandry staff to discuss appropriate animal care and use and share information.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the institution to comply with the PHS Policy on Humane Care and Use of Laboratory Animals.

Sincerely,

(b) (6)

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

cc: IACUC Chair



Covance Laboratories Inc.  
671 S. Meridian Road  
Greenfield, Indiana Tel:  
317/467-3700

October 1, 2018

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 Director:

I write to follow up on our preliminary notification to OLAW from September 18, 2018. Covance Laboratories with Assurance #A4683-01 provides this final report regarding two incidents involving rats found without access to food. On August 15, 2018, an IACUC Subcommittee Investigation was initiated according to our global policy on the reporting and investigation of animal welfare concerns.

**Incident One:**

One rat dam and a litter of 11 four-day-old pups were found without a feeder in the cage on July 27, 2018 during the morning health check. Per study records, the dam was observed to have piloerection, thin appearance, alopecia and hunched posture. Also per study records, nine rat pups were observed to be cold to touch and thin. Two pups were found dead.

The incident was reported to the Veterinary Staff and Study Director that same morning of July 27, 2018. The Study Director elected to forgo treatment and humanely euthanize the animals. This study is grant funded under contract (b) (4) Through Interinstitutional Assurance, Covance is conducting this study for the grant awardee.

1. The IACUC Subcommittee reviewed study data, operational processes, policies and SOPs, and also interviewed the staff involved in the incident. Study data shows that the animals were observed at least 5 times daily leading up to the discovery of the animals without food on July 27<sup>th</sup>:
  - AM Check (food and water access is checked directly).
  - Daily Pup mortality checks.
  - Daily Dam dosing
  - Daily Post Dose Observations
  - PM Check (food and water access is checked directly).

There was no data within the study records that showed any abnormal animals or any animals without food at any time prior to July 27<sup>th</sup>.

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Obtained by Rise for Animals. Uploaded 08/28/2020

Retrieved from Animal Research Laboratory Overview (ARLO)

2. Necropsy data review showed the dam lost approximately 40 grams from previous body weight. Per veterinary consult a lactating rat with a litter would have a high metabolism and could lose 40 grams in 24 hours or less.
3. Pup mortality is a possible outcome of reproduction study models, which is why Daily Pup Mortality checks are included in the study design. The IACUC is unable to determine if the death of the 2 pups was due to this incident or to expected pup mortality
4. Through interviews with technical staff involved it was found that some staff removed the feeder from the cage temporarily to fully visualize the dam and pups during animal health checks or dosing. There is a strong possibility that a feeder could have been removed and accidentally not returned due to this process.
5. Based on the clinical signs of the animals, veterinary consultation, staff interviews, and study data reviewed the evidence seems to support feeder was likely removed and accidentally not returned to the cage approximately 24 hours prior to animals being discovered without feed.

#### **Incident Two**

On August 11, 2018, 19 adult rats were found without feeders at the morning health check. The veterinarian examined the animals and found all animals to be bright, alert and responsive. Food pellets were placed on the cage floors and Diet Gel cups were given. The animals were removed from study eligibility and humanely euthanized.

1. The IACUC Subcommittee reviewed study data, operational processes, policies and SOPs, and also interviewed the staff involved in the incident.
2. Study data shows the animals were observed at least twice daily (AM and PM Checks) leading up to the discovery of the animals without food on August 11<sup>th</sup>. There was no data within the study records that show any abnormal animals or any animals without food at any time prior to August 11<sup>th</sup>.
3. These animals were in acclimation and were not being dosed. There were no scheduled activities for this room of animals other than AM and PM Checks.
4. Clinical observations recorded by the staff veterinarian who examined the animals on August 11<sup>th</sup> showed animals were not significantly impacted.
5. The evidence from this investigation supports the conclusion that animals were without food for a period of 24 hours or less which is supported by the absence of clinical signs observed in the animals that were examined by the staff veterinarian.

We currently have multiple processes in place to prevent animals from going without access to food including: SOPs, hands-on training, instructor-led training, a minimum of twice daily animal health checks and disciplinary policies outlining consequences of not following established processes pertaining to providing animals access to food. However we are committed to improving our animal program to prevent future occurrences.

The IACUC recommended the following corrective actions:

1. If the feeder does need to be moved for better access to the animals, the feeder should be hung on the front of the cage and not placed on any rack, cart or table. This will provide immediate visual reminder upon closing the cage door that the feeder has not been replaced, and thus help staff ensure that all feeders have been put back into the cage after activities. **Update** – This procedure was adopted and communicated to the staff on September 19, 2018.
2. The study technicians involved in this incident will be retrained on daily morning and evening health checks procedures for ensuring food and water access. **Update-** Study technician retraining was held on October 1, 2018.
3. Management should conduct regular reviews of daily health check data to ensure assigned tasks are being completed. The IACUC will monitor these reviews and the staff performance for a minimum of six months. **Update-** This activity has begun and will continue until April of 2019. If further incidences are discovered during this IACUC review period monitoring will be extended by the IACUC.
4. Additional signage should be added to animal rooms to serve as a reminder of tasks to be completed during AM and PM health checks, including ensuring animals have access to food and water. **Update-** Signage has been put in place.
5. Disciplinary action will be taken against any staff found to have failed to complete health checks according to established policies and SOPs. **Update-** Though the animals were left without feed there was not enough evidence to support disciplinary action against any individual. All staff involved in the incident will be retrained, per recommendation 2.
6. The IACUC Chair, Attending Veterinarian and Management will host open meetings with animal care staff to reiterate our expectations, our obligations and our commitment to the animals under our care. We will also use this opportunity to gather feedback from staff that will be used to help us improve our animal program. **Update-** The IACUC hosted an open meeting for staff in collaboration with Animal House Operations Management and site leadership on September 5, 2018. The meeting went very well and valuable feedback was gathered from staff. The plan is to continue these meetings regularly throughout the year to share information and gather feedback from staff.

Please contact Amanda Durnell (IACUC Chair) [amanda.durnell@covance.com](mailto:amanda.durnell@covance.com) or myself should you have any questions regarding this final report.

Sincerely,

(b) (6)

Steve Street  
Head, Early Development  
Institutional Official Covance  
Laboratories  
[Steve.Street@Covance.com](mailto:Steve.Street@Covance.com)

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Retrieved from Animal Research Laboratory Overview (ARLO)

## Morse, Brent (NIH/OD) [E]

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Tuesday, October 02, 2018 12:03 PM  
**To:** Street, Steve; OLAW Division of Compliance Oversight (NIH/OD)  
**Cc:** (b) (6) Durnell, Amanda  
**Subject:** RE: Division of Compliance Oversight

Thank you for this final report Mr. Street. 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

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**From:** Street, Steve [mailto:Steve.Street@covance.com]  
**Sent:** Tuesday, October 02, 2018 11:49 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** (b) (6) Durnell, Amanda <Amanda.Durnell@covance.com>  
**Subject:** Division of Compliance Oversight  
**Importance:** High

Dear Director

I write to follow up on our preliminary notification to OLAW from September 18, 2018, Covance Laboratories with Assurance #A4683-01, provides this final report as attached.

Sincerely

Steve Street  
Head, Early Development  
Institutional Official  
Covance Laboratories  
T (b) (6)  
M  
[www.covance.com](http://www.covance.com)

**COVANCE**  
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prelim.  
A4683-B

Covance Laboratories Inc.  
671 S. Meridian Road  
Greenfield, Indiana  
Tel: 317/467-3700

September 6, 2018

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 Director:

Covance Laboratories with Assurance #A4683-01 provides this report of noncompliance regarding two incidents involving rats found without access to food. On August 15, 2018, an IACUC Subcommittee Investigation was initiated according to our global policy on the reporting and investigation of animal welfare concerns.

**Incident One:**

1. One rat dam and a litter of 11 four-day-old pups were found without food in the cage on July 27, 2018 during the morning health check. Per study records, the dam was observed to have piloerection, thin appearance, alopecia and hunched posture. Also per study records, nine rat pups were observed to be cold to touch and thin. Two pups were found dead.
2. The incident was reported to the Veterinary Staff and Study Director that same morning of July 27, 2018. The Study Director elected to forgo treatment and humanely euthanize the animals.
3. The IACUC Subcommittee is reviewing study data and interviewing the staff, but is unable at this time to determine the length of time the dam was without access to food. However, data review showed the dam lost approximately 40 grams, which leads the veterinary team to estimate that the dam may have been without food for approximately 24-48 hours.
4. This study is grant funded under contract (b) (4). Through Interinstitutional Assurance, Covance is conducting this study for the grant awardee.
5. The IACUC Subcommittee Investigation is ongoing.



### **Incident Two:**

1. On August 11, 2018, nineteen adult rats were found without food at the morning health check. The veterinarian examined the animals and found all animals to be bright, alert and responsive. Food pellets were placed on the cage floors and Diet Gel cups were given.
2. The IACUC Subcommittee is actively reviewing study data and interviewing staff, but is unable at this time to determine the length of time the animals were without access to food.
3. The animals were removed from study eligibility and humanely euthanized.
4. The IACUC Subcommittee investigation is ongoing.

We currently have multiple processes in place to prevent animals from going without access to food including: SOPs, hands-on training, instructor-led training, a minimum of twice daily animal health checks and disciplinary policies outlining consequences of not following established processes pertaining to providing animals access to food.

The IACUC met August 29, 2018 to review the preliminary findings of these investigations. Based on the preliminary assessment, the following corrective and preventative actions will be taken immediately. Additional corrective actions may be implemented when the IACUC Investigation has concluded based on the results of that investigation.

1. The animal care staff involved in this incident will be retrained on daily morning and evening health checks procedures for ensuring food and water access.
2. Management will conduct regular reviews of daily health check data to ensure assigned tasks are being completed. The IACUC will monitor these reviews and the staff performance for a minimum of six months.
3. Additional signage will be added to animal rooms to serve as a reminder of tasks to be completed during AM and PM health checks, including ensuring animals have access to food and water.
4. Disciplinary action will be taken against any staff found to have failed to complete health checks according to established policies and SOPs.
5. The IACUC Chair, Attending Veterinarian and Management will host open meetings with animal care staff to reiterate our expectations, our obligations and our commitment to the animals under our care. We will also use this opportunity to gather feedback from staff that will be used to help us improve our animal program.

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Covance is committed to animal welfare and to making sure these incidents do not happen again and welcome any feedback you wish to provide at this time.

Please contact Amanda Durnell (IACUC Chair) [amanda.durnell@covance.com](mailto:amanda.durnell@covance.com) or myself should you have any questions regarding this preliminary report. We will provide a further update once the IACUC committee investigation is completed.

Sincerely,

(b) (6)  


Steve Street  
Head, Early Development  
Institutional Official  
Covance Laboratories  
[Steve.Street@Covance.com](mailto:Steve.Street@Covance.com)

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## Morse, Brent (NIH/OD) [E]

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Tuesday, September 18, 2018 1:29 PM  
**To:** Street, Steve; OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: Division of Compliance Oversight

Thank you for providing this preliminary report Mr. Street. We will open a case file and await further information as noted in your letter.

Best regards, Brent Morse

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

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**From:** Street, Steve [mailto:Steve.Street@covance.com]  
**Sent:** Tuesday, September 18, 2018 11:15 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Subject:** Division of Compliance Oversight  
**Importance:** High

Dear Director

Please find attached letter which serves as a preliminary report of noncompliance for Covance Laboratories Assurance #A4683-01.

Sincerely

Steve Street  
Head, Early Development  
Institutional Official  
Covance Laboratories

T (b) (6)

M

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