



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) 480-3387

April 17, 2020

Re: Animal Welfare Assurance  
A3629-01 [OLAW Case K]

Dr. Joseph Heppert  
Vice President for Research and Innovation  
TTU Institutional Official  
Texas Tech University  
Box 41075  
Lubbock, Texas 79409

Dear Dr. Heppert,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your April 14, 2020 memorandum in response to the March 17, 2020 letter from the Office of Laboratory Animal Welfare (OLAW).

The memorandum states that the IACUC did not identify any noncompliance issues with the event reported by the investigator to the committee. However, in reviewing the summary of events that were described, this Office considers the events as incidents of noncompliance. Based on the January 24, 2020 letter it is understood that one pig displayed agonal breathing and died following oral gavage, and a second pig (with the Attending Veterinarian present) displayed similar signs following gavage and was euthanized. The letter stated the AV performed on the spot training and no issues were observed with the remaining pigs. On December 17, 2019 oral gavage challenge was performed again on pigs with a clinical veterinarian present that did not note any technical deficiencies. Subsequently, one pig was found dead the following day (it is noted this animal did receive veterinary treatment) and was submitted for necropsy. Also, two additional pigs displayed respiratory distress on December 18<sup>th</sup>, and one was euthanized and submitted for necropsy. Post-mortem findings were similar for both animals and described as esophageal perforation and foreign substance present within the thoracic cavity. The necropsy findings (in addition the deaths from September) indicate to this Office that research staff were not proficient in the technique of oral gavage in pigs, and therefore in noncompliance with the PHS Policy. The PHS Policy states the IACUC shall determine that the research project meets specific requirements. One of the requirements identified in IV.C.1.f. states "Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures." At a minimum, the PHS Policy and the *Guide* require institutions to:

- ensure that individuals who use or provide care for animals are trained and qualified in the appropriate species-specific housing methods, husbandry procedures, and handling techniques;
- ensure that research staff members performing experimental manipulation, including anesthesia and surgery, are qualified through training or experience to accomplish such procedures humanely and in a scientifically acceptable fashion

The memorandum states that oral gavage will be used to administer peanut proteins only if animals do not voluntarily consume solid treats. It's further stated that if oral gavage is necessary then the lab group will be retrained by veterinary staff and supervised until deemed proficient.

Based on its assessment of this explanation, OLAW understands that Texas Technical University has implemented appropriate measures to correct and prevent recurrences of these problems and is now compliant with provisions of the PHS Policy. Please note, any future problems (e.g. injured or dead pigs) with this project should be promptly reported to OLAW.

Sincerely,

(b) (6)

Jacquelyn T. Tubbs, DVM  
Veterinary Medical Officer  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare

cc: IACUC Contact



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March 17, 2020

Re: Animal Welfare Assurance  
A3629-01 [OLAW Case K]

Dr. Joseph Heppert  
Vice President for Research and Innovation  
TTU Institutional Official  
Texas Tech University  
Box 41075  
Lubbock, Texas 79409

Dear Dr. Heppert,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your January 24, 2020 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Texas Tech University.

According to the information provided, this Office understands that the Texas Tech University Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to: unexpected deaths in swine on an approved protocol. On September 9, 2019 research personnel initiated oral gavage challenge in pigs. Shortly after gavage, a pig exhibited agonal breathing, was given oxygen, but did not recover. University veterinarians were contacted about the incident and the Attending Veterinarian (AV) observed a second pig to undergo the same challenge. Once again, similar agonal breathing occurred after gavage, the animal was given oxygen, showed no improvement and was euthanized. The AV conducted on the spot retraining and discussed methods to ensure the tubing was in the esophagus and not the trachea. These steps were followed, and succeeding pigs were gavaged without incident.

On December 17, 2019 oral gavage challenge was performed on pigs. The clinical vet observed the gavage procedure and did not note any technical deficiencies. Immediately after gavage, the pigs were lethargic, which is an anticipated outcome to having allergic response to the peanut. All pigs were rechecked at 8h post procedure, and one pig was found open mouth breathing and cyanotic. The clinical veterinarian was called and provided treatment, but the animal did not completely return to normal. The following day, the animal was found dead and sent to the diagnostic lab for testing. Two other pigs were identified the morning of December 18, 2019 as having increased respiration and lethargy and they were treated as well. On December 20, 2019 one of the two pigs had increased respiration return and the clinical vet decided to euthanize and necropsy. The third pig recovered without incident. Diagnostics on the first pig indicated the esophagus has been perforated and a foreign substance was within the thoracic cavity. The necropsy on the second pig revealed the same complications reported from diagnostics. The AV sent an email to the PI and appropriate personnel on December 20, 2019 ceasing oral gavage activity since this was a recurring incident. Based on the AV recommendations, personnel would investigate tubing options and/or other delivery methods for pigs to voluntarily consume peanut. They will also investigate alternative delivery methods or decrease the volume and viscosity of the substance gavaged.

On March 9, 2020 a memorandum was received with the PI's response/update to the IACUC. The PI provided an update to the committee on the revised oral delivery methods to pigs. It stated formulations will be administered to pigs as solid dosage forms. These forms will include banana pancakes, frozen banana cubes, cookies, etc. Due to animal preference, there will be flexibility in the offering of treats. Swine will be acclimated and habituated to the receipt of treats. To increase cooperation of the pigs in eating treats, pigs will be fasted the night before the procedure when the actual formulation will be included in the treat. If despite fasting, the pig does not eat the solid treat, PI will use oral gavage with reduced volume. The viscosity of the solution used in the oral gavage will be lowered as compared to what has been used in the past.

It is noted that the final report did not include the funding source involving the incident. In the future, please include the source of funding and provide grant numbers for all PHS or NSF supported work. Based on the information provided, the Office of Laboratory Animal Welfare (OLAW) understands that the principal investigator will use alternative delivery methods in pigs, but it is unclear if these treats will contain peanut or not. Please clarify. The investigator also states that if pigs do not eat solid treats then oral gavage with reduced volume will be used. The necropsy findings included esophagus perforation in one pig and similar findings in a second. PHS Policy IV.C.1.f. states "Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures." The IACUC must verify that personnel on the protocol are trained and *proficient* in all techniques, particularly, oral gavage in this circumstance. **Please provide a status update to this Office by June 30, 2020.** Please note, should any other problems (e.g. injured or dead pigs) occur prior to the requested date, they should be promptly reported to OLAW.

Sincerely,

(b) (6)

Jacquelyn T. Tubbs, DVM  
Veterinary Medical Officer  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare

cc: IACUC Contact  
Robert M. Gibbens, DVM, Director, Animal Welfare Operations

**MEMORANDUM**

March 09, 2020

TO: OLAW, AAALAC (b) (6)  
FROM: Dr. Joseph Heppert, IO  
CC: TTU IACUC; (b) (6)  
RE: Final Resolution for Unexpected Deaths for Protocol 18007-01

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This memo is in response to the email dated 2/4/2020 from J Tubbs to TTU IACUC (see attached) where we were informed that a case file had been opened for this incident. Please see the attached memo from the PI to the IACUC. This memo was discussed during the IACUC's monthly meeting on March 5, 2020. We consider this to be a final resolution to this incident. If you have any questions or need anything additional information, please do not hesitate to contact me.

## **Institutional Animal Care and Use Committee**

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**From:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Sent:** Friday, January 31, 2020 11:55 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD)  
**Cc:** Institutional Animal Care and Use Committee  
**Subject:** RE: Texas Tech University Unexpected Deaths for Protocol 18007-01

Good afternoon,

I just wanted to follow up and state a case file has been opened. We will await your final report.

Kind Regards,

J Tubbs

**From:** Tubbs, Jai (NIH/OD) [E] <jacquelyn.tubbs@nih.gov>  
**Sent:** Wednesday, January 29, 2020 7:36 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Subject:** FW: Texas Tech University Unexpected Deaths for Protocol 18007-01

**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Wednesday, January 29, 2020 7:35 AM  
**To:** 'Institutional Animal Care and Use Committee' <iacuc@ttu.edu>  
**Subject:** RE: Texas Tech University Unexpected Deaths for Protocol 18007-01

Good morning,

Thank you for the report. We will send an official response soon.

Kind Regards,

Jacquelyn Tubbs, DVM, DACLAM  
Veterinary Medical Officer  
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.





TEXAS TECH UNIVERSITY

Edward E. Whitacre Jr.  
College of Engineering

*Chemical Engineering*  
March 9, 2020

Harvinder Singh Gill, Ph.D.  
Associate Professor of Chemical Engineering  
Whitacre Endowed Chair in Science and Engineering  
Texas Tech University  
8th and Canton, Mail Stop 3121  
Lubbock, TX 79409-3121  
Ph: 806-834-3682  
Email: [harvinder.gill@ttu.edu](mailto:harvinder.gill@ttu.edu)  
Laboratory website: [www.gilllab.science](http://www.gilllab.science)

**Re: Final resolution on addressing unexpected deaths of pigs on protocol 18007-01**

Dear IACUC of Texas Tech University

Guided by the results of our studies in pigs in which pigs were fed with different solid dosage forms, we will adopt the following oral delivery procedures in this protocol.

- Formulations will be administered to pigs as solid dosage forms. These will be in the form of banana pancakes, frozen banana cubes, cookies etc. Sometimes an individual pig may prefer a different treat, so we will be flexible in offering treats. To get the pigs accustomed to eating these treats, we will feed treats to pigs even when there is no active formulation ingredient added to the treat. This will habituate and train the pigs to readily eat treats when offered.
- To increase the cooperation of the pigs in eating the treats, pigs will be fasted the night before the procedure when the actual formulation will be included in the treat.
- If despite fasting, the pig does not eat the solid treat, we will use oral gavage with reduced volume (maximum 15 ml, which is 4-fold lower as compared to about 60 ml, which we have been using in the past). Importantly, the viscosity of the solution used in the oral gavage will be lowered as compared to what has been used in the past. This will help in the oral gavage procedure.

No amendment is required since overnight fasting and administration of different oral treats are already approved.

Please let me know if you have additional questions.

Best regards and sincerely,

 (b) (6)

**Wolff, Axel (NIH/OD) [E]**

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Friday, March 13, 2020 1:03 PM  
**To:** Institutional Animal Care and Use Committee  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: Final Resolution for Unexpected Deaths for Protocol 18007-01

Thank you for this report, (b) (6) Dr. Tubbs will reply soon.

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

**From:** Institutional Animal Care and Use Committee <iacuc@ttu.edu>  
**Sent:** Friday, March 13, 2020 12:33 PM  
**To:** 'accredit@aaalac.org' <accredit@aaalac.org>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** Heppert, Joseph <Joseph.Heppert@ttu.edu>; (b) (6)

(b) (6)

**Subject:** Final Resolution for Unexpected Deaths for Protocol 18007-01

Hello,

Please see the attached memo and supporting documents.

(b) (6)



**Tubbs, Jai (NIH/OD) [E]**

---

**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Friday, January 31, 2020 12:55 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD)  
**Cc:** Institutional Animal Care and Use Committee  
**Subject:** RE: Texas Tech University Unexpected Deaths for Protocol 18007-01

Good afternoon,

I just wanted to follow up and state a case file has been opened. We will await your final report.

Kind Regards,

J Tubbs

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**From:** Tubbs, Jai (NIH/OD) [E] <jacquelyn.tubbs@nih.gov>  
**Sent:** Wednesday, January 29, 2020 7:36 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Subject:** FW: Texas Tech University Unexpected Deaths for Protocol 18007-01

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Wednesday, January 29, 2020 7:35 AM  
**To:** 'Institutional Animal Care and Use Committee' <iacuc@ttu.edu>  
**Subject:** RE: Texas Tech University Unexpected Deaths for Protocol 18007-01

Good morning,

Thank you for the report. We will send an official response soon.

Kind Regards,

Jacquelyn Tubbs, DVM, DACLAM  
Veterinary Medical Officer  
Office of Laboratory Animal Welfare  
National Institutes of Health

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A3629-K

**Tubbs, Jai (NIH/OD) [E]**

---

**From:** Tubbs, Jai (NIH/OD) [E]  
**Sent:** Wednesday, January 29, 2020 7:36 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** FW: Texas Tech University Unexpected Deaths for Protocol 18007-01

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**To:** 'Institutional Animal Care and Use Committee' <iacuc@ttu.edu>  
**Subject:** RE: Texas Tech University Unexpected Deaths for Protocol 18007-01

Good morning,

Thank you for the report. We will send an official response soon.

Kind Regards,

Jacquelyn Tubbs, DVM, DACLAM  
Veterinary Medical Officer  
Office of Laboratory Animal Welfare  
National Institutes of Health

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---

**From:** Institutional Animal Care and Use Committee <iacuc@ttu.edu>  
**Sent:** Tuesday, January 28, 2020 3:24 PM  
**To:** 'accredit@aaalac.org' <accredit@aaalac.org>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>

**Cc:** [REDACTED] (b) (6) (b) (6)

**Subject:** Texas Tech University Unexpected Deaths for Protocol 18007-01

Hello,

Please see the attached document.

(b) (6)



MEMORANDUM

January 24, 2020

To: AAALAC, OLAW

From: Dr. Joseph Heppert, IO

CC: TTU IACUC; (b) (6)

RE: Unexpected Deaths for Protocol 18007-01

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This memo is to report unexpected deaths on protocol 18007-01 at Texas Tech University.

On 9/11/2019 research personnel initiated oral gavage challenge on pigs. Soon thereafter the pig exhibited agonal breathing. The pig was provided oxygen, but it did not recover. Immediately upon observance of agonal breathing, University veterinarians were contacted regarding the incident, and the Attending Vet (AV) went to the facility to observe the pig. The AV observed a second pig undergo the gavage procedure, and similar agonal breathing occurred. Once again, the pig was put on oxygen with no improvement, it was euthanized by CO<sub>2</sub>. It was determined that both pigs aspirated the experimental material which resulted in agonal breathing. The AV conducted on-the-spot retraining. The AV also discussed methods to ensure the tubing was in the esophagus and not the trachea. These steps were followed, and the succeeding pigs were gavaged without incident.

On 12/17/2019 research personnel performed an oral gavage challenge on pigs. Once in the esophagus they slowly pushed 20g peanut flour in 65ml volume at 5ml increments to observe the pig swallowing and breathing before pushing more volume. The clinical vet through post approval monitoring observed the gavage procedure and did not note any technical deficiencies. Immediately after gavage, the pigs were lethargic, which is part of the expected outcome to having an allergic response to the peanut. Approximately eight hours post procedure, all pigs were rechecked. One pig was found to have open mouth breathing and was cyanotic (possible symptoms of anaphylaxis). The clinical veterinarian was called and consulted on treatment. The pig was treated with 0.1cc Epinephrine in case it was the beginning of anaphylaxis, and 1cc dexamethasone. Color came back immediately and breathing slightly improved but did not completely return to normal. On 12/18/2019 at 8:30 A.M. the pig was found dead. The pig was sent to a diagnostic lab for diagnostics testing. Two other pigs were also identified on the morning of 12/18/2019 as having increased respiratory rate and lethargy,

and were treated with 1cc dexamethasone and breathing improved. Diagnostics on the first pig were received late on 12/19/2019 indicating that the esophagus had been perforated and a foreign substance was within the thoracic cavity. On 12/20/2019, one of the two additional pigs' increased respiration rate returned and the clinical vet decided to euthanize and necropsy. Results showed the same complications reported from diagnostics. The third pig recovered without incident.

The AV sent an email to the PI and appropriate personnel on 12/20/2019 ceasing oral gavage activity on protocol 18007-01 since this was a recurring incident. The AV recommended the following:

1. Concentrate the peanut allergen and find another way to administer orally, i.e. in a palatable treat, capsule or bolus
2. Different method of administration, i.e. IP injection
3. If oral gavage must be done, decrease the volume and viscosity of the substance. Find a more appropriate gavage tube and use an oral gag.

Personnel are currently looking into tubing options, or other delivery methods for pigs to voluntarily consume the peanut. Additionally, they will investigate other ways to change the method of delivery or decrease the volume and viscosity of the substance gavaged.