University of Louisville

Institutional Animal Care and Use Committee

Meeting Minutes

Thursday, 17 September 2020, 9:00 AM

Teleconference

Members Present:	**Members Absent:**	**Additional Attendees:**
Dr. Pascale Alard		Ms. Stacy Cantrell
Dr. Geoffrey Clark		Dr. Steven Davison
Dr. Cynthia Corbitt		Dr. Katie Emmer
Dr. Swati Joshi-Barve		Ms. Brigitte Foote
Dr. Amanda LeBlanc		Dr. Torsten Hopp
Dr. Ben Lovely		Ms. Keisha Navarrete
Dr. David Magnuson		Ms. Tegan Tulloch
Dr. Kenneth Palmer		
Dr. George Pantalos		
Dr. Karen Powell		
Dr. Mary Proctor		
Dr. Leslie Sherwood		
Dr. David Samuelson		
Ms. Kathleen Smith		
Dr. Sucheta Telang		

I. Call to Order and Approval of the Minutes from the Previous Monthly Meeting, 20 August 2020 (Attachment 1)

Dr. Pantalos called the meeting to order at 9:06 AM with 15 voting members present.

The minutes from the previous meeting were presented for review. *A motion to accept the minutes was* ***unanimously approved*** (*15 "in favor," none opposed, no abstentions*).

Ms. Navarrete, a visiting veterinary student from LMU, was introduced to the Committee.

II. Ratification of Approved *Proposals* (Attachment 2)

All Committee members had an opportunity to individually review "Proposals to Use Laboratory Animals in Research and Teaching" (*Proposals*) presented for IACUC approval. *The following proposals were ratified with all eligible votes in favor and abstentions due to a conflict of interest for the following:* 19500 (Palmer), 19628 (Magnuson), 20711 (Boakye [Sherwood]), 20754 (Barve [Joshi-Barve]), 20799 (Pantalos), and 20802 (Kosiewicz [Alard]).

New Proposals: 18211 19494 20804

Three Year Renewals: 20753 20754 20799 20802 20813

Modifications: 18377 18418 19469 19500 19524 19534 19545 19568 19606 19628 19647 19660 19661 19665 20706 20709 20711 20743

Annual Review: None.

Tissue: None.

Administrative Modification: 17080 18216 19545 20726 20727 20764 20772

III. Continuing Education, Policy Review, iRIS Improvements

A. "Breeding without research," *Lab Animal*, 39:2 (*Sherwood*) (**Attachment 3**)
Dr. Sherwood presented this article that included a scenario about an investigator breeding and euthanizing amphibians without conducting the research described and approved in his IACUC proposal. The Committee discussed the 3 Rs and appropriate breeding colony maintenance.

IV. Open Discussion / Full Committee Review – *None*

V. Old Business

A. Follow Up Report: *Proposal* 20706, "Model development for emerging human coronaviruses in the ferret" (*Powell, Emmer*) – *No Report Expected*
There is no update at this time; the IACUC has not yet received a follow-up report from the investigator. None has been expected since they have not completed another study.

B. Humane Endpoints Proposal 19657 (*Pantalos*) (**Attachments 4 and 5**)
The Principal Investigator provided preliminary data regarding the use of Whole Body Plethysmography to refine endpoints and correlate lung function with disease severity. The progress has been delayed by custom construction of the equipment, equipment calibration, and an unexpected infection in the breeding colonies.

C. Humane Endpoints Proposal 19498 (*Pantalos, Sherwood*) (**Attachment 6**)
The Principal Investigator's response to the IACUC's follow up letter on humane endpoint refinement and development was included for the Committee's information. The investigator stated that the current bacterial load analysis studies aim to define post-infection timepoints and will not alter the established humane endpoint criteria. The Committee was perplexed, as the IACUC approved the humane endpoints last year with the understanding that these endpoints would be the subject of further analysis and refinement during the bacterial load analysis studies. A subcommittee consisting of Drs. Pantalos, Palmer, Powell and Sherwood will investigate the matter further and reach out to the investigator.

D. PETA Open Records Request (*Pantalos, Sherwood*)
Items V(D) and VI(D) were discussed simultaneously. Dr. Pantalos has contacted Sherry Pawson to obtain the official response to PETA's open record request, but has been unable to connect with her. He will visit her office at Ekstrom Library this month. PETA's recent news releases calling for the shut down of UofL animal labs and a state audit of university animal research were included for the Committee's information. Dr. Sherwood noted that PETA is sending similar letters, submitting FOIA requests and is requesting audits of institutions across the country. Included in the attachments were talking points that Dr. Sherwood helped draft in response to PETA's accusations. However, the UofL Department of Communication decided to not respond to the Courier Journal's request for comment at this time.

VI. New Business

A. Semi-Annual Report to the Institutional Official, *Preliminary (Pantalos, Sherwood)* (**Attach. 7**)
The Committee reviewed and approved the preliminary report to the Institutional Official with the following changes: the expired buprenex finding should be labeled significant; the ketamine inside the refrigerator finding should be labeled minor; and the unavailable laboratory records finding should be changed to minor as records were made available after the inspection. The Committee agreed that due to the gravity of one laboratory's finding that involved administering post-operative analgesia in a manner not approved on the IACUC *Proposal* (via canine oral meloxicam placed on food), the members of the laboratory responsible for administering analgesia will be required to attend a training session with Dr. Davison.

A motion to accept the preliminary semiannual report to the Institutional Official with the above changes ***was unanimously approved*** (12 "in favor," none opposed, no abstentions). The IACUC Office will add signatures electronically to the letter to the Institutional Official for all of the members present.

B. USDA APHIS Inspection (*Sherwood*)
Due to the COVID-19 pandemic, the annual USDA inspection will be a focused visit consisting of a virtual document review. The inspection is currently underway and concludes this afternoon.

C. December IACUC Meeting (*Sherwood*)
Due to the current pandemic, the annual holiday luncheon is being postponed. The IACUC will attempt a celebratory luncheon meeting at a later date when it is safe to do so.

D. PETA News Release and Letter to KY State Auditor (*Sherwood*) (**Attachment 8**)
This item was discussed simultaneously with V(D).

E. Other Business
Dr. Pantalos informed the Committee that the Red Cross HSC blood drive is scheduled for October 7 between 9 a.m. – 3 p.m. in the CII.

VII. Adjournment

The IACUC was reminded that the next meeting will occur via teleconference Thursday, 17 September 2020 at 9:00 a.m. *Meeting was adjourned at 10:28 AM.*

Investigator	Protocol	Original Approval	Submission Approval	Expiration	Species	Pain Class	Animals Approved
Wysoczynski, Marcin	IACUC 17080	2019-05-13 00:	2020-08-31 00:	2022-05-12 00:	Mouse (Laboratory)	2	4180
Admin Mod - Study Site Change					**Reviewer:**	Tulloch, Tegan N	
Innate immunity in heart repair							
Guo, Haixun	IACUC 18211	2020-08-31 00:	2020-08-31 00:	2023-08-30 00:	Mouse (Laboratory)	2	600
Initial Review					**Reviewer:**	Joshi-Barve, Swati - Designated	
Combined therapy on cancer mouse model							
Gomes, Cynthia	IACUC 18216	2018-06-27 00:	2020-09-10 00:	2021-06-26 00:	Mouse (Laboratory)	2	2154
Admin Mod - Funding Change					**Reviewer:**	Tulloch, Tegan N	
Mapping of sensory innervations in spinal cord and peripheral organs after complete transection injury of spinal cord in mice.							
Ding, Dale	IACUC 18377	2019-01-25 00:	2020-08-21 00:	2022-01-24 00:	Mouse (Laboratory)	2	670
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Effects of MerTk antagonism on Intracerebral and Subarachnoid Hemorrhage							
Kirpich, Irina	IACUC 18418	2019-01-09 00:	2020-08-19 00:	2022-01-08 00:	Mouse (Laboratory)	3	2160
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
The role of dietary fat in alcoholic liver disease							

Investigator	Protocol	Original Approval	Submission Approval	Expiration	Species	Pain Class	Animals Approved
Tang, Xian-Liang	IACUC 19469	2019-07-24 00:	2020-09-14 00:	2022-07-23 00:	Rat (Laboratory)	2	644
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	

Cardiac function, survival and repair after myocardial infarction in rats

Worley, Micah J	IACUC 19494	2020-08-19 00:	2020-08-19 00:	2023-08-18 00:	Mouse (Laboratory)	2	3638
Initial Review					**Reviewer:**	Corbitt, Cynthia, Ph.D. - Designated	

The entry of Salmonella-infected cells into the bloodstream

Palmer, Kenneth E	IACUC 19500	2020-04-10 00:	2020-08-31 00:	2023-04-09 00:	Mouse (Laboratory)	3	650
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	

Evaluation the antiviral potential of Q-Griffithsin (Q-GRFT) against influenza (H1N1 strain) in a mouse model

Lawrenz, Matthew B	IACUC 19524	2019-08-08 00:	2020-08-20 00:	2022-08-07 00:	Mouse (Laboratory)	3	7740
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	

Yersinia pestis Virulence and Therapeutic Studies (ABSL-3)

Lawrenz, Matthew B	IACUC 19524	2019-08-08 00:	2020-08-25 00:	2022-08-07 00:	Mouse (Laboratory)	3	7740
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	

Yersinia pestis Virulence and Therapeutic Studies (ABSL-3)

Investigator	Protocol	Original Approval	Submission Approval	Expiration	Species	Pain Class	Animals Approved
Conklin, Daniel	IACUC 19534	2019-10-17 00:	2020-08-24 00:	2022-10-16 00:	Mouse (Laboratory)	2	5544
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
General Inhalation Protocol							
Cai, Jun	IACUC 19545	2020-06-16 00:	2020-08-31 00:	2023-06-15 00:	Mouse (Laboratory)	3	2585
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Neuronal and oligodendroglial modulations on axonal regeneration in the CNS							
Cai, Jun	IACUC 19545	2020-06-16 00:	2020-08-31 00:	2023-06-15 00:	Mouse (Laboratory)	3	2585
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Neuronal and oligodendroglial modulations on axonal regeneration in the CNS							
Siskind, Leah J	IACUC 19568	2019-10-28 00:	2020-09-08 00:	2022-10-27 00:	Mouse (Laboratory)	3	1367
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Role of ceramides in acute kidney injury							
Jala, Venkatakrishna R	IACUC 19606	2019-11-06 00:	2020-09-03 00:	2022-11-05 00:	Mouse (Laboratory)	3	9953
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Copy of Role of Gut microbitoa in inflammatory disorders							

Investigator	Protocol	Original Approval	Submission Approval	Expiration	Species	Pain Class	Animals Approved
Magnuson, David S	IACUC 19628	2019-11-04 00:	2020-09-09 00:	2022-11-03 00:	Rat (Laboratory)	2	192
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Treating rats like people after SCI							
Hill, Bradford G	IACUC 19647	2020-01-24 00:	2020-09-08 00:	2023-01-23 00:	Mouse (Laboratory)	2	11971
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Interventions for obesity, CVD, and diabetes							
McGee, Aaron W	IACUC 19660	2020-02-24 00:	2020-08-28 00:	2023-02-23 00:	Mouse (Laboratory)	2	5806
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Regulation of neuronal plasticity by myelin-associated inhibitors							
Srivastava, Sanjay	IACUC 19661	2019-12-18 00:	2020-08-31 00:	2022-12-17 00:	Mouse (Laboratory)	2	4958
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Impact of VOCs exposure on cardiometabolic disease							
McCall, Maureen A	IACUC 19665	2020-01-31 00:	2020-08-31 00:	2023-01-30 00:	Pig (Domestic)	2	640
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Gene therapy for blinding eye diseases							
Severson, William E	IACUC 20706	2020-02-28 00:	2020-09-03 00:	2023-02-27 00:	Ferret	3	117
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Model development for emerging human coronaviruses in the ferret							

Investigator	Protocol	Original Approval	Submission Approval	Expiration	Species	Pain Class	Animals Approved
Severson, William E	IACUC 20706	2020-02-28 00:	2020-09-14 00:	2023-02-27 00:	Ferret	3	121
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Model development for emerging human coronaviruses in the ferret							
Deng, ZhongBin	IACUC 20709	2020-06-05 00:	2020-09-08 00:	2023-06-04 00:	Mouse (Laboratory)	3	2620
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Intestinal epithelial cells-derived exosomes regulate liver and gut inflammation and cancer							
Boakye, Maxwell	IACUC 20711	2020-04-01 00:	2020-09-08 00:	2023-03-31 00:	Pig (Domestic)	2	24
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Epidural Stimulation Improvement of Neurogenic Bowel After Acute Spinal Cord Injury - A Large-Animal Study							
Moore, Joseph B	IACUC 20726	2020-05-14 00:	2020-08-26 00:	2023-05-13 00:	Mouse (Laboratory)	2	9150
Admin Mod - Emergency Contacts Update					**Reviewer:**	Tulloch, Tegan N	
Functional studies of lncRNAs regulated in cardiovascular disease							
Moore, Joseph B	IACUC 20727	2020-06-01 00:	2020-08-26 00:	2023-05-31 00:	Mouse (Laboratory)	2	15000
Admin Mod - Emergency Contacts Update					**Reviewer:**	Tulloch, Tegan N	
Functional studies of RNA editing events in cardiovascular disease							
Severson, William E	IACUC 20743	2020-04-21 00:	2020-09-14 00:	2023-04-20 00:	Hamster, Syrian	3	1687
Modification					**Reviewer:**	Pantalos, George - Designated/Chair Signoff	
Coronavirus disease in hamsters for antiviral testing							

Investigator	Protocol	Original Approval	Submission Approval	Expiration	Species	Pain Class	Animals Approved
Ratajczak, Mariusz	IACUC 20753	2020-09-08 00:	2020-09-08 00:	2023-09-07 00:	Mouse (Laboratory)	3	254
3YR					**Reviewer:**	Magnuson, David S, Ph.D. - Designated	
The role of sterile inflammation and purinergic signaling in trafficking of stem cells							
Barve, Shirish S	IACUC 20754	2020-08-20 00:	2020-08-20 00:	2023-08-19 00:	Mouse (Laboratory)	3	16092
3YR					**Reviewer:**	Corbitt, Cynthia, Ph.D. - Designated	
Renewal of IACUC#15251: The Role of Gut Microbiome in Alcohol-Induced liver injury and Neuroinflammation.							
Carll, Alex P	IACUC 20764	2020-08-14 00:	2020-08-20 00:	2023-08-13 00:	Mouse (Laboratory)	2	7296
Admin mod - Study Site Change					**Reviewer:**	Tulloch, Tegan N	
Air Pollution and Heart Failure							
O'Toole, Timothy E Admin Mod - Study Site Change	IACUC 20772	2020-07-27 00:	2020-08-31 00:	2023-07-26 00:	Mouse (Laboratory)	2	3436
					Reviewers:	Tulloch, Tegan N	
Endothelial Progenitor Cells and Particulate Air Pollution							
Pantalos, George	IACUC 20799	2020-08-25 00:	2020-08-25 00:	2023-08-24 00:	Pig (Domestic)	2	102
3YR					**Reviewer:**	Magnuson, David S, Ph.D. - Designated	
Copy of Porcine Model Lung Harvest for Ex Vivo Lung Perfusion and Preservation							
Kosiewicz, Michele M	IACUC 20802	2020-09-09 00:	2020-09-09 00:	2023-09-08 00:	Mouse (Laboratory)	2	2340
3YR					**Reviewer:**	Telang, Sucheta - Designated	
Sex-based differences in autoimmune disease							

Investigator	Protocol	Original Approval	Submission Approval	Expiration	Species	Pain Class	Animals Approved
Diamond, Gill	IACUC 20804	2020-08-26 00:	2020-08-26 00:	2023-08-25 00:	Mouse (Laboratory)	1	312
Initial Review					**Reviewer:**	Corbitt, Cynthia, Ph.D. - Designated	
Topical Vitamin D and Periodontal Disease							
Warawa, Jonathan M	IACUC 20813	2020-09-10 00:	2020-09-10 00:	2023-09-09 00:	Mouse (Laboratory)	2	2400
3YR					**Reviewer:**	Magnuson, David S, Ph.D. - Designated	
Breeding Protocol							

Jerald Silverman, DVM, Column Coordinator

Breeding without research

Sometimes an animal breeding protocol is like an overflowing bathtub: water continues to flow in and spill out, but the amount of water in the tub stays the same. Dr. Jonathan Spencer had a breeding colony of *Xenopus* frogs that was like the bathtub. Animals came and went, but all of the available tanks were always occupied. Kyle Sawyer, the animal facility supervisor, suspected that something was amiss because he never saw any requests to transfer frogs from Spencer's breeding protocol to his research protocol. After talking with the animal care technicians, Sawyer found that many frogs had been euthanized on Spencer's request. He asked the technicians what they thought the problem might be, and they quickly responded that there was no problem at all. Spencer continued to breed the frogs and then euthanize them when space ran out. This had been going on for more than a year. So Sawyer delved deeper. He found that Spencer's IACUC protocols were approved for breeding nearly 1,000 frogs over a 3-year period and that he was approved to use half of them (females) for his research needs. Not knowing how to proceed, Sawyer went to the chairman of his IACUC.

Sawyer's basic concern was that frogs were being bred and euthanized but not used for research. He considered this a waste of life and wanted the IACUC to check Spencer's breeding and experimental records because the animal care technicians said that both males and females were being euthanized. The chairman understood Sawyer's concern and was sympathetic but noted that Spencer had an approved protocol for breeding and that the euthanasia method was approved by the IACUC; in general, he felt that the IACUC should investigate concerns only when there was evidence of protocol noncompliance or animal abuse. In his opinion, neither had occurred. Nevertheless, he said he would bring the matter to the IACUC at its next meeting.

Before the full committee meeting was held, the IACUC determined that the observations of the animal care technicians were accurate. Spencer was breeding and euthanizing frogs and not using them for his approved research. When Spencer himself was questioned, he said that he had experienced some unforeseen delays but that he would start using the animals in the near future. What do you think this IACUC should do now in light of the facts presented?

RESPONSE

Spirit of the 3Rs

Gail Colbern, DVM, MS, DACT &
Cheryle Aird, RVT, LATG, CPIA

Spencer wrote his protocol, had it approved and followed the procedures outlined in the protocol for breeding his frogs. The only problem is that he isn't doing the research that he outlined and justified in his IACUC protocol. Although Spencer's frogs are not covered by the provisions of the Animal Welfare Act, generally all IACUC protocols require "identification and appropriateness of the species and number of animals to be used"[1,2]. The principle of the 3Rs applies specifically to "procedures that can cause more than slight or momentary pain or distress in animals, consistent with sound research design"[3] and thus would not limit Spencer's breeding program. The description of the research project, as outlined in the original protocol, however, is clearly not being followed.

This situation, as Sawyer has pointed out, also does not follow the spirit of the 3Rs in reducing the total number of animals used. When Sawyer discovered the situation, he correctly requested the breeding and research records. The approved protocol allows Spencer to breed 1,000 frogs per year and to use half of them, or all of the females, in his research. If he has reached his breeding quota for the year, he must return to the IACUC for approval and justification for additional breeding to take place. As justification would require adequate description of the use of the first 1,000 frogs, the situation would be clearly defined for the IACUC. The IACUC could then determine whether 'unforeseen delays' constitute sufficient justification for Spencer to continue breeding these animals and, if so, for how much time or how many frogs.

Another consideration not specifically stated in the scenario is who is paying for this project. At a pharmaceutical company, Spencer may have to answer only to his supervisor and upper management for spending money to breed frogs that were not needed or used. This might reflect badly in his performance evaluation. If, however, the frog breeding was being done with grant funding, then the institution, not the IACUC, is responsible for ensuring that funds are spent as outlined in the grant. If grant funds were being spent to breed and maintain frogs that were not used to complete the funded research, then the granting agency would expect the institution to report the inappropriate use of its funds, at the least. This could be considered grant fraud and, depending on the granting agency, may be pursued in other ways beyond the scope of this protocol review.

Sawyer was correct in questioning the ongoing breeding of frogs when no research was being done. This situation clearly violates the spirit of the principle of minimizing the waste of animal life. Sawyer was also protecting his institution by reporting a situation where funds may have been used inappropriately.

1. Animal Welfare Act, 9 CFR Chapter 1, Section 2.31 (1997).

2. Silverman, J., Suckow, M.A. & Murthy, S. *The IACUC Handbook* 2nd edn. 158 (CRC Press, Boca Raton, FL, 2007).
3. Office of Laboratory Animal Welfare. *Institutional Animal Care and Use Committee Guidebook* 2nd edn. 97 (US Department of Health and Human Services, Washington, DC, 2002, reprinted 2008).

Colbern is Consulting Veterinarian with Cave Cancri, Pacifica, CA, and Aird is Vivarium Manager at Takeda San Francisco, South San Francisco, CA.

RESPONSE

Safeguard the 3Rs

Deepti Chadalavada, DVM

The IACUC has the responsibility to safeguard the 3Rs (reduction, refinement and replacement) recommended by the Public Health Service *Policy on Humane Care and Use of Laboratory Animals* and the *Guide for the Care and Use of Laboratory Animals*[1,2]. The Public Health Service *Policy* and USDA Animal Welfare Regulations[3] require research institutions and IACUCs to ensure that investigators have appropriately considered alternatives for animals in their research and are using the minimum number of animals by avoiding unintended breeding. It also suggests that to minimize the loss of animals, investigators should plan ahead and use appropriate statistical analysis in order to breed the number of animals necessary to obtain maximum information with minimal loss of life. It is the responsibility of the IACUC to ensure that such measures have been taken and that investigators are in full compliance with the regulations. It is also the responsibility of the IACUC to help assure high standards of animal welfare in the institution[4]. In this case, even though frogs are not a species covered by the USDA, the IACUC chairman cannot deny that this is indeed an IACUC issue of potential animal waste. Thus, the IACUC should be informed of the situation and the concern of the animal resources staff and should take appropriate action.

The IACUC should consider halting Spencer's frog breeding protocol until an appropriate resolution is developed to minimize the unnecessary waste of animals. The Dean or Chair of the Department should be notified about the current situation and the IACUC action. Future work on the animals (frogs) under this protocol should be resumed only after obtaining permission of the IACUC by demonstrating to the committee that all of Spencer's "unforeseen" problems are resolved. Any future protocols

A word from OLAW and USDA

In response to the issues raised in this scenario, the Office of Laboratory Animal Welfare (OLAW) and the United States Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care (USDA, APHIS, AC) offer the following clarification and guidance:

The Public Health Service *Policy on Humane Care and Use of Laboratory Animals* is applicable to live vertebrate animals used in research, research training and biological testing and clearly applies to amphibians bred and used for research[1]. The *Policy* does not explicitly require an institutional mechanism to track animal usage by investigators in IACUC-approved activities, but it does require proposals to specify and to include a rationale for the number of animals to be used and requires that number to be limited to the minimum necessary to obtain valid results. Accordingly, institutions need to appropriately monitor and document numbers of animals acquired (through breeding or other means) and used in approved activities. Monitoring should not exclude the disposition of animals that are inadvertently or necessarily produced in excess of the number needed or that do not meet criteria (e.g., sex) established for the specific study proposal[2].

The mandate in US Government Principle III to use the minimum number of animals necessary to obtain valid results is synonymous with a requirement to reduce animal numbers, which is one of the 3Rs[3,4]. IACUCs, acting as agents of institutions, are expected to implement and routinely evaluate this aspect of the institutional animal care and use program to ensure compliance with the PHS *Policy*. When deviations from the approved number of animals occur, the IACUC should review the circumstances, take appropriate action to correct any noncompliance and report to OLAW and the funding agency as applicable.

The Animal Welfare Act[5] defines an animal as "any live or dead dog, cat, nonhuman primate, guinea pig, hamster, rabbit, or any other warm-blooded animal, which is being used, or is intended for use for research, teaching, testing, experimentation, or exhibition purposes, or as a pet. This term excludes birds, rats of the genus Rattus, and mice of the genus Mus, bred for use in research; horses not used for research purposes; and other farm animals, such as, but not limited to, livestock or poultry used or intended for use as food or fiber, or livestock or poultry used or intended for use for improving animal nutrition, breeding, management, or production efficiency, or for improving the quality of food or fiber. With respect to a dog, the term means all dogs, including those used for hunting, security, or breeding purposes."

Although the *Xenopus* frogs discussed in this scenario are not covered under the Animal Welfare Regulations[5], the policies and procedures implemented by the IACUC must continue to ensure that proposals utilizing all covered species are in compliance with the Animal Welfare Regulations.

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals — Frequently Asked Questions.* Animal Use and Management, Question No. F.2. (US Department of Health and Human Services, Washington, DC, 2006, revised 2009).
3. Interagency Research Animal Committee, Office of Science and Technology Policy. U.S. Government principles for the utilization and care of vertebrate animals used in testing, research, and training. *Federal Register* **50**, 864–902 (1985).
4. Russell, W.M.S. & Burch, R.L. *Principles of Humane Experimental Techniques* (Methuen and Co., London, 1959).
5. Code of Federal Regulations, Title 9, Chapter 1, Subchapter A - Animal Welfare: Part 1 Definitions. (§1.1).

Patricia Brown, VMD, MS, DACLAM
Director
OLAW, OER, OD, NIH, HHS

Chester Gipson, DVM
Deputy Administrator
USDA, APHIS, AC

from Spencer should be approved only after the investigator has proven his competency and demonstrated to the IACUC that he has resolved all problems of animal waste by appropriate implementation of the 3Rs. Spencer should assure the IACUC that he is capable of minimizing the number of frogs in his breeding colony by providing good records of the numbers of animals bred, offspring produced and animals used. It is highly advisable that the IACUC monitor Spencer's work closely in the future to assure compliance with the regulations and the general intent of the 3Rs (to minimize the number of animals used in research, teaching and breeding protocols).

In summary, the role of IACUC in this situation is to oversee the breeding on a regular basis, to track the numbers of animals bred and used in the research, to evaluate the approved protocols during their semiannual inspections and to take necessary steps to correct any deficiencies.

1. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* (National Academies Press, Washington, DC, 1996).
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
3. Silverman, J., Suckow, M.A. & Murthy, S. *The IACUC Handbook* 2nd edn. 158 (CRC Press, Boca Raton, FL, 2007).
4. Office of Laboratory Animal Welfare. *Institutional Animal Care and Use Committee Guidebook* 2nd edn. 97 (US Department of Health and Human Services, Washington, DC, 2002).

Chadalavada is Lab Animal Medicine Fellow at City of Hope/Beckman Research Institute, Duarte, CA.

RESPONSE

Letter versus intent

Kimberly A. Overhulse, RVT, RLATG, CMAR & Eric Nelson, DVM, DACLAM

Spencer may be in compliance with the protocol approved by the IACUC, but we feel that this situation seriously deviates from one of the principles of the 3Rs (reduction). There is no direct use of the 3Rs, as presented by Russell and Burch[1], in the guidelines and regulations from our main regulatory bodies (USDA and OLAW), but the use of this principle is inferred. For instance, the *Guide for the Care and Use of Laboratory Animals*[2] endorses the *US Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*[3], which lists "use of appropriate species, quality, and number of animals." The 3R principles define reduction as the "minimum number of animals that will serve a useful purpose, yield statistically sound data and produce scientific benefit"[1]. OLAW has indicated that federal mandates in US Government Principles III and IV are synonymous with the principles of the 3Rs and that the 3Rs should be incorporated into IACUC review and other aspects of the institution's program[4]. Spencer's breeding activities as currently conducted unnecessarily increase the number of animals needed to eventually carry out the studies that are outlined. In our opinion, this practice is irresponsible and unacceptable. We believe that it is not in line with the objectives and mission of the IACUC.

In light of the facts presented, we feel that the IACUC should ask Spencer to cease breeding until he is prepared to transfer the animals to research studies. If he cannot cease breeding completely in order to maintain the colony, then the minimum level of breeding should be maintained and alternative uses for the unneeded animals should be sought, such as transfer to a different lab or even another institution. The IACUC should consider setting a policy for the management of animals that are 'in house' during a hiatus from activity, including breeding colonies.

1. Russell, W.M.S. & Burch, R.L. *Principles of Humane Experimental Techniques* (Methuen and Co., London, 1959).
2. National Research Council. Committee to Revise the *Guide for the Care and Use of Laboratory Animals, Guide for the Care and Use of Laboratory Animals* (National Academies Press, Washington, DC, 1996).
3. Public Health Service. *US Government Principles for Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training* (US Department of Health and Human Services, Washington, DC, 2002).
4. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* – Frequently Asked Questions. Protocol Review Question No. 7. (US Department of Health and Human Services, Washington, DC, 2006; revised 2009).

Overhulse is the Training Coordinator for Laboratory Animal Sciences and IACUC member and Nelson is the Director of Laboratory Animal Sciences at Allergan Inc., Irvine, CA.

Institutional Animal Care and Use Commit

From: Warawa,Jonathan Mark
Sent: Friday, August 28, 2020 12:31 PM
To: Pantalos,George; Institutional Animal Care and Use Commit
Cc: Sherwood,Leslie C
Subject: RE: IACUC 19567 Follow Up
Attachments: IACUC letter updating on respiratory endpoint.pdf

Follow Up Flag: Follow up
Flag Status: Flagged

George,
Yes, sorry again for delays. We weren't happy with the calibration approach until recently. We now have an approach that allows our equipment to be calibrated in a way that holds reproducibly over months.

We also have a big problem with co-infections in our mice. We breed all our own study animals and picked up a Staphylococcus saprophyticus infection that ruins our course of disease. The problem has not resolved itself over several months of problem solving. This bacterial species is a major causative agent for UTIs, so my technician necropsied retiring breeders and has found it up in the kidneys. Dr. Powell apparently has been unable to confirm this for us with sentinel mice, but again, the problem hasn't gone away and we still have mice going down without our normal levels of bioluminescent bacteria in the lung.

The data I am providing is from a study before we encountered our Staph issue, and I think the use of WBP is very promising. We of course would like to confirm the n=1 finding, and I detail all of this in the letter.
Have a great weekend,
Jon

Jonathan Warawa, PhD
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jonathan.warawa@louisville.edu

From: Pantalos,George <george.pantalos@louisville.edu>
Sent: Wednesday, August 26, 2020 4:15 PM
To: Warawa,Jonathan Mark <jonathan.warawa@louisville.edu>; Institutional Animal Care and Use Commit <iacuc@louisville.edu>
Cc: Sherwood,Leslie C <leslie.sherwood@louisville.edu>
Subject: RE: IACUC 19567 Follow Up

Hi, Jon!

I wanted to check in since you sent this message. Any progress on you being able to analyze and share your data?

Good Luck!

George

From: Warawa,Jonathan Mark <jonathan.warawa@louisville.edu>
Sent: Monday, July 20, 2020 2:03 PM
To: Institutional Animal Care and Use Commit <iacuc@louisville.edu>
Cc: Pantalos,George <george.pantalos@louisville.edu>; Sherwood,Leslie C <leslie.sherwood@louisville.edu>
Subject: RE: IACUC 19567 Follow Up

Tegan,
We haven't forgotten about this request. This is custom equipment and I have been working with the vendor of the digital equipment side on the best way to calibrate our system. We have archived data which we have to analyze in retrospect. I think we are close to settling on the best way to do this, and we hope to then have a dataset for the IACUC in the next couple of weeks.
Best,
Jon

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From: Institutional Animal Care and Use Commit <iacuc@louisville.edu>
Sent: Monday, July 20, 2020 1:44 PM
To: Warawa,Jonathan Mark <jonathan.warawa@louisville.edu>
Cc: Pantalos,George <george.pantalos@louisville.edu>; Sherwood,Leslie C <leslie.sherwood@louisville.edu>
Subject: IACUC 19567 Follow Up
Importance: High

Good Afternoon Dr. Warawa,

Please see the attached letter from the IACUC in regard to your Proposal 19567. If you have any questions, please let us know.

Best Regards,

Tegan

Center for Predictive Medicine
for Biodefense and Emerging Infectious Diseases
UNIVERSITY OF LOUISVILLE

August 28, 2020

George Pantalos, PhD
IACUC Chairman
University of Louisville

Re: Update of use of respiratory criteria as endpoint criteria for respiratory melioidosis (19567)

Dr. Pantalos,

I previously wrote an update letter to the IACUC about use of temperature endpoints in our model, and I presented data about the lack of consistency in how mice develop hypothermia as a response to respiratory melioidosis. In some instances we observe a consistent drop in temperture, but in other studies the animals rapidly become hypothermic and hold a reduced temperature for days on end (not predictive). We proposed to investigate use of Whole Body Plethysmography to non-invasively monitor breathing in mice to attempt to correlate some measure of lung function to disease severity.

I was asked to provide data from 3 studies. At the moment I am afraid I can provide data only from a single study, and I do not want to delay providing at least some data to the IACUC after several follow up requests. Some of the issues we have encountered include custom construction of our own WBP equipment, learning how best to calibrate the equipment for the small volume breathing of mice, and an unfortunate infection problem of our breeding colonies. Recent studies have picked up contamination of the lungs of study mice with *Staphylococcus saprophiticus* which affect the course of disease in our respiratory studies (morbidity with no bioluminescence in the lung), and we have been able to culture this contaminant from the kidneys of mice in our breeding colonies. We have consulted with Dr. Powell about this contamination, and she has been unable to confirm breeding colony contamination, though we are persistently identifying this contaminant in our study mice.

We believe we at least have one good study which was not affected by the *Staphyococcus* contaminant. We include data from the female control group of a study testing IL-12 therapy, which experienced a typical course of disease. The data page attached to this letter has a panel of 5 figures. The top two figures present the data we have typically collected in our studies, looking at the in vivo bioluminescence measurement from the lung (thoracic cavity) and the subcutaneous transponder temperature measurement. All mice in this study were euthanized at 69 hr post infection. We observe the typical log-growth of bioluminescent bacteria in the lung, and a hypothermia response from the host. Note, we do not always observe the steady onset of hypothermia observed in this study, and the IACUC was briefed on this data earlier this year.

We then looked at the various measurements related to breathing in these mice. Breathing frequency (measured in hertz) declines rapidly and remains low for days until the mice are euthanized, thus this is

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not a predictive measurement. Conversely, breath volume remains high until the mice begin to approach a full course of disease; this may allow for a predictive measurement. Finally, a 'traditional' measure of lung function is the Minute Volume, which we calculated from breath frequency and breath volume. The final figure shows that the minute volume decreases more steadily over time and that an argument could be made for use of 1 ml/min as being an appropriate endpoint criteria for lung function.

Interestingly, the temperature data and minute volume data very closely follow one another's trend, even including the brief plateau of mouse 488 at the 21 hr time point (purple data set) in both temperature and minute volume. We believe that minute volume could represent an excellent endpoint criteria for our respiratory disease work, particularly because it is an non-invasive technique which requires only briefly placing a mouse into a WBP jar (<1 minute) before returing to its cage.

Our one reservation about immediately adapting 1 ml/min minute volume as an endpoint criteria is that this is predicated off of one study with which we are confident. We are currently resolving our Staphylococcus infection problem, and would appreciate the patience of the IACUC while we address that problem and analyze additional positive control group data. In the study data we provided, the onset of hypothermia was gradual, which we know is not a consistent finding of our work. Ideally we would like to observe a study where hypothermia is not gradual, but the minute volume data remains predictive.

Best regards,

Jonathan Warawa, Ph.D.
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Department of Microbiology and Immunology
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Louisville, KY 40202
Tel: 502-852-5558
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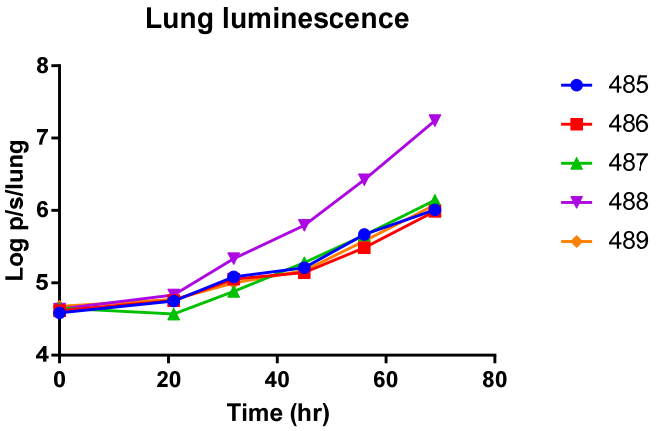
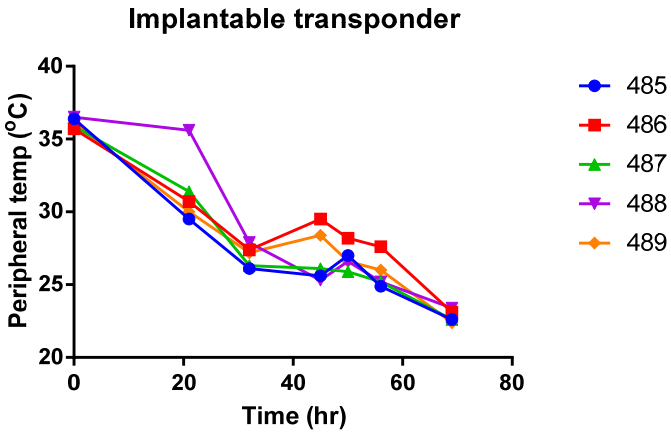
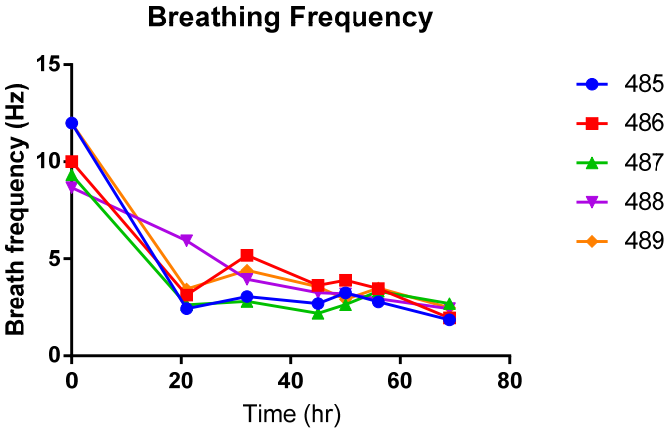
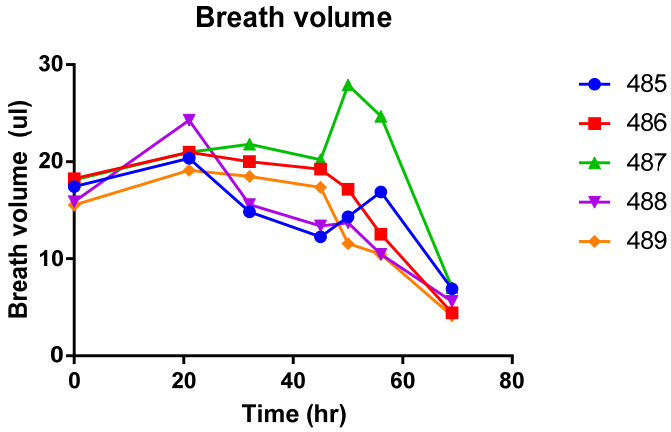
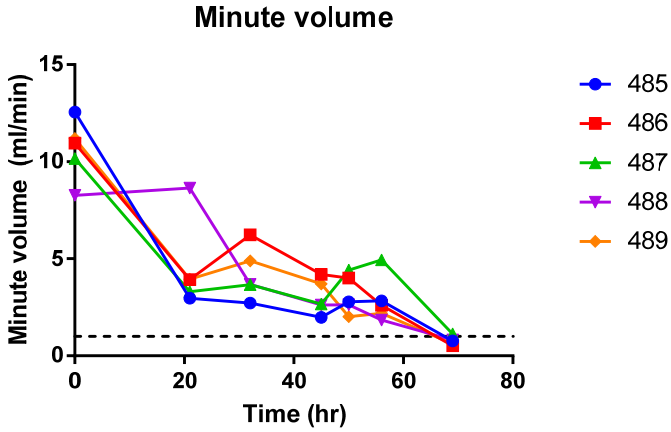
Attachment: Analysis of female albino C57BL/6 mice infected with ~10^5 CFU WBP014











From: Lawrenz,Matthew B <matt.lawrenz@louisville.edu>
Sent: Wednesday, September 02, 2020 11:25 AM
To: Pantalos,George <george.pantalos@louisville.edu>
Cc: Sherwood,Leslie C <leslie.sherwood@louisville.edu>; Warawa,Jonathan Mark <jonathan.warawa@louisville.edu>
Subject: RE: Pseudomonas Humane Endpoints

George,
Studies analyzing bacterial load do not change our humane endpoint criteria. Essentially, these studies have defined timepoints post-infection in which animals are euthanized. Our window of time for these types of studies was chosen based on previous studies that established the approximate time animals reached endpoint criteria. For example, if we established in previous studies that strain A reaches our established humane endpoint criteria at 24 h, then groups will be euthanized at 3, 6, 12, and 21 h post-infection to determine bacterial proliferation and dissemination. So, while it does minimize pain and suffering, as we do not wait until the development of terminal disease to quantify bacterial numbers, it does not change our established humane endpoint criteria.

Please also note that for these studies we still monitor the animals every 8 h for the development of disease and we would euthanize any animals that reach endpoint criteria prior to designated timepoints if needed. However, we have performed 5 such studies since May 2019 and have not needed to euthanize any animals using this study design because they met endpoint criteria (n= 44 per experiment, 220 total, 0 euthanized because they met endpoint criteria).

Hopefully this helps to clarify how this type of experiment can minimize pain and discomfort, but does not directly impact, or inform about, established human endpoint criteria.

-Matt

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http://louisville.edu/predictivemedicine
http://louisville.edu/medicine/departments/microbiology
<image001.png>
[redacted]

From: Pantalos,George
Sent: Wednesday, September 02, 2020 10:13 AM
To: Lawrenz,Matthew B <matt.lawrenz@louisville.edu>
Cc: Sherwood,Leslie C <leslie.sherwood@louisville.edu>
Subject: RE: Pseudomonas Humane Endpoints

Matt:

We were under the impression that you would have done some of the work on bacterial load that was proposed in order to be able work toward modifying the humane endpoints? Possibly that has not happened or possibly we misunderstood what was going to happen?

Cheers, Matt!

George

From: Lawrenz,Matthew B <matt.lawrenz@louisville.edu>
Sent: Tuesday, September 01, 2020 4:26 PM
To: Pantalos,George <george.pantalos@louisville.edu>
Subject: RE: Pseudomonas Humane Endpoints

George,
Our endpoints have not changed, but I am not sure what information the IACUC is looking for in this query. Can you provide some guidance?

-Matt

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http://louisville.edu/medicine/departments/microbiology
<image004.png>
[redacted]

From: Institutional Animal Care and Use Commit
Sent: Tuesday, September 01, 2020 4:03 PM
To: Lawrenz,Matthew B <matt.lawrenz@louisville.edu>
Cc: Sherwood,Leslie C <leslie.sherwood@louisville.edu>; Pantalos,George <george.pantalos@louisville.edu>
Subject: Pseudomonas Humane Endpoints

Good Afternoon Dr. Lawrenz,

Please see the attached letter from the IACUC requesting an update on your humane endpoint development for the P. aeruginosa infection studies. Please let us know if you have any questions.

Best,

Tegan

George M. Pantalos, Ph.D.
Chair
Institutional Animal Care and Use Committee (IACUC)

17 September 2020

Toni M. Ganzel, M.D., M.B.A.
Dean, School of Medicine
Institutional Official, Animal Care and Use Program
University of Louisville
Louisville, KY 40292

Dear Dr. Ganzel:

[redacted]

DRAFT/unsigned

[redacted]

[redacted]

Sincerely,

George Pantalos, PhD
IACUC Chair

University of Louisville, Louisville, KY 40292
P: 52.852.7307 **F**:502-852.7943

Pascale Alard, PhD	Kenneth Palmer, PhD
Geoffrey Clark, PhD	Karen Powell, DVM, MS, PhD
Cynthia Corbitt, PhD	Mary Proctor, DVM, MS, DACLAM
Swati Joshi-Barve, PhD	David Samuelson, PhD
Amanda LeBlanc, PhD	Leslie Sherwood, DVM
Ben Lovely, PhD	Kathleen Smith, BA
David Magnuson, PhD	Sucheta Telang, MD
Cheri Hildreth, MBA	Torsten Hopp, PhD

Institutional Animal Care and Use Commit

From: Sherwood,Leslie C
Sent: Tuesday, September 15, 2020 1:53 PM
To: Institutional Animal Care and Use Commit
Subject: Fw: PETA and UofL Talking Points
Attachments: Talking Points - Animal welfare-lcs_9-11-20.docx

Follow Up Flag: Follow up
Flag Status: Flagged

From: Sherwood,Leslie C
Sent: Monday, September 14, 2020 3:40 PM
To: Ganzel,Toni Michelle <toni.ganzel@louisville.edu>; Gardner,Kevin <kevin.gardner@louisville.edu>
Cc: Pantalos,George <george.pantalos@louisville.edu>
Subject: PETA and UofL Talking Points

Good afternoon,

As you may already be aware, last Thursday PETA released a press announcement and the Courier Journal ran a story on it (links below). Betty Coffman sent me a draft of talking points in case the university decides to respond at some point. I edited them and sent them back to her (attached). Nothing to do at the moment but I'm keeping you in the loop. We are not alone and they are targeting institutions across the country with similar propaganda.

https://www.peta.org/media/news-releases/covid-19-prompts-peta-call-for-university-of-louisville-to-shut-down-animal-labs/

https://www.courier-journal.com/story/news/2020/09/10/peta-asks-audit-of-university-louisville-over-animal-killing-allegations/5761357002/

Best,

Leslie

COVID-19 Prompts PETA Call for University of Louisville to Shut Down Animal Labs

Experimenters Told That 'All Non-Essential Research Activities Are Suspended' as Part of COVID-19 Response Plan

For Immediate Release:
April 17, 2020

Contact:
Tasgola Bruner 202-483-7382

Louisville, Ky. – Because of the COVID-19 outbreak, the University of Louisville has told experimenters that "all non-essential research activities are suspended" and that "[n]on-essential research studies and experiments that have not yet started should be immediately postponed," which likely will lead to the killing of hundreds or more animals.

PETA fired off a letter today (https://www.peta.org/wp-content/uploads/2020/04/COVID-19_Urgent_Request_to_University_of-Louisville_04172020.pdf) to the university's president, Neeli Bendapudi, demanding to know why the school conducts noncritical animal experiments. PETA is also alerting the public to email the university via this Action Alert (https://support.peta.org/page/18416/action/1) to urge transparency in how many animals the school deems nonessential and euthanizes in response to COVID-19 and to stop all current and new animal experiments.

The University of Louisville needs to stop all current and new animal experiments, ban the breeding and purchase of animals, and switch to superior, human-relevant research methods. The school also needs to tell taxpayers how many animals it deemed extraneous and killed in response to COVID-19.

"The University of Louisville's use of intelligent animals in experiments as though they were nothing more than disposable laboratory equipment is shameful," says PETA Vice President Shalin Gala. "The COVID-19 pandemic should be a moral and scientific reckoning for the school, which conducts deadly experiments on animals it keeps in small steel cages. If it can't prove that these experiments on animals are essential—which by taking this action, they are saying they are not —it must not be permitted to continue squandering taxpayer money on inessential business-as-usual, once the pandemic is over."

Numerous published studies have shown that animal experimentation wastes resources and lives, as more than 90% of highly promising results from basic scientific research—much of it involving animal experimentation—fail to lead to treatments for humans. (Please read under “Lack of benefit for humans” here (https://www.peta.org/wp-content/uploads/2020/03/bmj-is-animal-research-sufficiently-evidenced-basede-tobea-cornerstone-of-biomedical-research.pdf).) And 95% of new medications that are found to be effective in animals fail in human clinical trials. (https://ncats.nih.gov/files/NCATS_Factsheet_508.pdf)

PETA—whose motto reads, in part, that “animals are not ours to experiment on”—opposes speciesism, which is a human-supremacist worldview. For more information, please visit **PETA.org** (https://www.peta.org/) or **click here** (https://www.peta.org/blog/coronavirus-animal-killing-spree-college-labs/).

PETA’s letter to the university is available here (https://www.peta.org/wp-content/uploads/2020/04/COVID-19_Urgent_Request_to_University_of-Louisville_04172020.pdf).

(https://www.peta.org/media/contact-media-department/)

Contact PETA's Media Department

CONTACT (HTTPS://WWW.PETA.ORG/MEDIA/MEDIA-DEPARTMENT/)

Also of Interest

Join PETA’s Action Team to Help Animals (https://www.peta.org/action/action-team/)

Order Your FREE Vegan Starter Kit! (https://www.peta.org/living/food/free-vegan-starter-kit/)

Vegan Recipes (https://www.peta.org/recipes/)

courier journal

NEWS

PETA asks for state audit of University of Louisville over animal killing allegations

Sarah Ladd Louisville Courier Journal

Published 12:46 p.m. ET Sep. 10, 2020 | **Updated 5:11 p.m. ET Sep. 11, 2020**

People for the Ethical Treatment of Animals is asking Kentucky Auditor Mike Harmon to audit the University of Louisville over allegations of animal killings.

In a Wednesday letter, Shalin Gala, vice president of PETA's International Laboratory Methods, asked Harmon to audit money and other resources including property, equipment and staff used for animal experimentations that were not deemed essential during the coronavirus pandemic.

Gala cited a March 24 letter from Kevin H. Gardner, the vice president for research and innovation at the university, instructing all researchers to decrease nonessential research and postpone any nonessential research that hadn't yet begun.

"These directives likely led to the destruction of hundreds of animals UL deemed extraneous, noncritical or nonessential or described using similar terminology," wrote Gala, who also accused U of L of using state dollars on animal experiments that aren't necessary.

A university spokesman did not respond to a request for comment.

More news: Part of Anti-Racism Agenda, U of L School of Medicine faculty pledge $50,000 for scholarships

Read this: U of L student group calls on university to cut ties with LMPD, Aramark

A spokesman for Harmon's office said the letter was received Wednesday afternoon and that staff are reviewing it.

"However, at first glance it appears the corrective actions they are requesting would be outside the authority of the Office of the Auditor of Public Accounts and would be more

properly directed to the members of the Kentucky General Assembly," said spokesman Michael Goins.

Those corrective actions include ensuring "current state-funded research activities involving such animals are permanently terminated, that new state-funded research activities that include such animals are no longer approved, and that the breeding and acquisition of such animals for state-funded research activities are prohibited."

Reach breaking news reporter Sarah Ladd at sladd@courier-journal.com. Follow her on Twitter at @ladd_sarah. Support strong local journalism by subscribing today: courier-journal.com/subscribe.