

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE
REPORT REGARDING THE STATUS
OF MICHIGAN STATE UNIVERSITY'S ANIMAL CARE PROGRAM
January 2022
(Reporting Period: 07/01/21 - 12/31/21)

The Michigan State University (MSU) Institutional Animal Care and Use Committee (IACUC) conducts semiannual reviews of its animal care and use program and submits reports of the evaluations to the Institutional Official (IO), the Vice President for Research and Innovation. The IACUC manages and evaluates the Animal Care Program in compliance with USDA regulations (9 CFR Parts 1, 2, & 3), the *Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy)*, the *Guide for the Care and Use of Laboratory Animals, 8th Edition (the Guide)*, and the *Guide for the Care and Use of Agricultural Animals in Research and Teaching, 3rd Edition (Ag Guide)*. MSU is registered with the United States Department of Agriculture as an institution that has USDA-regulated species on its premises. The University has an approved Animal Welfare Assurance (A3955-01) from the NIH Office of Laboratory Animal Welfare (OLAW). In addition, all components of the University are accredited by AAALAC International.

EVALUATION OF THE ANIMAL CARE AND USE PROGRAM

The IACUC uses various methods to perform the Semiannual Program Review to focus on topics of importance and to analyze the program in different manners such as using the OLAW checklist and reviews of our PHS Assurance and AAALAC program Description. Importantly, the IACUC reviews the program on a monthly basis during the IACUC meetings. On December 9, 2021, the IACUC evaluated the Animal Care Program (ACP) through a robust discussion of two articles covering topics germane to the role of the IACUC to ensure animal welfare:

- "Documentation on personnel training" *Lab Animal*, Volume 50, November 2021
- "Training the trainee: the institution's responsibility to the often forgotten" *Lab Animal*, Volume 34, No. 6, June 2005

IACUC members concluded that these articles served as an excellent training module for the committee by providing a review of the role of the IACUC in animal use and oversight in research and teaching by ensuring ethical, scientifically sound, standardized, and performance-based practices. Members were confident that MSU's program appropriately addresses these points and meets or exceeds standards. The broad membership of our IACUC facilitates the ability to review effectively research and teaching procedures that cover a diverse range of biomedical, wildlife, and agricultural topics.

The IACUC also reviewed MSU's animal care program in terms of what constitutes a program that has a direct impact on the well-being of animals, including animal and veterinary care, policies and procedures, personnel and program management and oversight, occupational health and safety, IACUC functions, and animal facility design and management. Information in the *Guide* served as a discussion point. The committee continues to be satisfied with the way our institution has continued to provide effective and continued care and wellbeing of animal use.

Program Review Conclusion

During the Program Review, no deficiencies in the IACUC practices and procedures were

identified and all aspects of the program were found to be consistent with the PHS Policy, the *Guide*, the *Ag Guide*, and applicable Animal Welfare Regulations. The committee concluded that the program is satisfactory.

INSPECTION OF ANIMAL FACILITIES

The IACUC inspected the animal facilities during the month of October, using the *Guide*, *Ag Guide*, and, as applicable, 9 CFR Parts 1, 2, & 3. The IACUC inspects housing facilities in the spring and fall of each year. Laboratories/study areas are inspected every six months on a rotating basis according to the buildings in which they are located. Due to the continuing pandemic and safety restrictions in place 113 inspections were performed in person and 8 via zoom. Personnel from EHS participated in the inspections.

Inspection Conclusions:

The results of the facility inspections revealed minor deficiencies at various animal sites as shown in the attached inspection summary (pages 4-5). All deficiencies are monitored until corrected as described in the following paragraph.

Monitoring deficiencies identified during inspections and/or post-approval monitor visits:

Notifications about the deficiencies are sent to the department chairpersons/directors and/or facility supervisors with a date for completing the correction of any deficiencies. Instructions for resolution can include notification in writing to the IACUC indicating that the deficiencies have been corrected or that a plan of action is in place for correcting the deficiencies. The Research Liaison (Postapproval Monitor) follows up on all deficiencies, verifies corrections, and reports directly to the IACUC. Should the deficiency be elevated to a significant concern, the Animal Care Program leadership will meet with the investigator and research team involved, and there may be increased visits to the laboratory and facilities to monitor corrective actions through to completion. The IACUC Oversight Committee provides assistance with amendments/changes to protocols and practices for approved animal work.

COMMITTEE MEMBERSHIP

The membership of the committee has changed since the last semiannual report. The complete IACUC roster is on page 6.

EXCEPTIONS TO THE GUIDE

As required by regulation, a list of IACUC-approved (July-December) exceptions to the Guide are included on pages 7-9.

IACUC RECOMMENDATIONS TO THE IO:

UPDATE on July 2021 Report:

Resource planning is underway for the following:

- Click System Upgrade will improve PI use of the system, efficiency of protocol review, and reporting capabilities thereby reducing burden. Definition of additional continuing technical resources to support the next system upgrade are in process. Of note, the upgrade is required

- prior to installing the new Animal Operations module.
- New Click Module, Animal Operations. The Click Animal Operations module will provide significant advantages to efficiency and data management over the existing CARLOS (Campus Animal Resources Laboratory Ordering System). To date, through coordination with ORA, ITS (Leadership, Purchasing, Project Management) and the software vendor a draft of the purchasing agreement is being developed for final approval.

We are pleased to report that the critical staffing changes within the ACP went smoothly: in addition to the new Assistant VP Office of Regulatory Affairs (McCabe), IACUC Administrator (Wilkins) and Interim Attending Veterinarian (Ferguson) joined the team.

When the institutional collaboration with the Henry Ford Health System moves forward, the leadership of the animal care program will be available to develop processes to align the two programs.

The IACUC recognizes that the needs of an animal care program are constantly changing and require a great deal of effort and persistence to implement. Further, the IACUC and the Oversight Committee are committed to providing excellence and transparency in our program to the biomedical and agricultural communities at MSU. We appreciate all the support that the administration has given to the Animal Care Program

MINORITY VIEWS

There are no minority views submitted at this time.

Michigan State University
IACUC Semiannual Fall 2021
Facility and Laboratory Inspections

Building Number	Species	Date	Inspection findings	Deficiency: Acceptable=A Minor=M Significant=S	Room Location	Date to be Corrected	Correction Confirmation Date	Comments, EHS, PAM
■	Rodents	10/12/2021	Found expired eye lubricant and lanolin	M	■	4/30/2022	10/12/2021	
■	Rodents	10/12/2021	Cages under PI care- no PI care sheet being used- no food in cages- no way to tell when the animals last had food Container of chow on counter- unlabeled Discarded day of inspection	M	■	4/30/2022	10/12/2021	
■	Rodents	10/12/2021	Found expired saline, isopropanol and 70% ethanol	M	■	4/30/2022	10/12/2021	
■	Rodents	10/12/2021	Protocol number expired 03/18-037-00	M	■	4/30/2022	10/12/2021	
■	Rodents	10/12/2021	Mice cages- tag indicates OVX done- no analgesic indicated on surgical card (3 cages) (PROTO201900103)	M	■	4/30/2022	11/11/2021	
■	Rodents	10/12/2021	Found expired meloxicam	M	■	4/30/2022	12/2/2021	
■	Rodents	10/13/2021	Found expired vetbond	M	■	4/30/2022	11/23/2021	
■	Rodents	10/13/2021	Found expired virkon and bleach solution Found expired sunflower seeds (disposed of at time of inspection); expired bleach solution and hazard label needed on bleach	M	■	4/30/2022	10/13/2021	
■	Rodents	10/13/2021	Fighting cage of mice- at least one animal wounded and bleeding- animals were separated during inspection and vet card completed	M	■	4/30/2022	10/13/2021	
■	Mice, Rats, Cats, Dogs, Pigs	10/19/2021	Found expired surgical lubricant, charcoal canister weights needed if in use.	M	■	4/30/2022	10/19/2021	
■	Large Animals	10/19/2021	Found expired corn starch.	M	■	4/30/2022	11/17/2021	

Michigan State University
IACUC Semiannual Fall 2021
Facility and Laboratory Inspections

Building Number	Species	Date	Inspection findings	Deficiency: Acceptable=A Minor=M Significant=S	Room Location	Date to be Corrected	Correction Confirmation Date	Comments, EHS, PAM
█	Small Animals	9/27/2021	Expired controlled drugs were found and need to be segregated and labeled as such. They also should be marked that they cannot be used on any animal terminal or survival. These drugs CANNOT be used for terminal procedures. Segrated and labeled for disposal at time of inspection.	M	█	3/1/2022	9/27/2021	
█	Small Animals	10/19/2021	Treats must be stored in a secondary container when opened. Contained during inspection.	M	█	4/22/2022	10/19/2021	
█	Rodents	7/28/2021	Found expired Isoflurane. Laboratory disposed of and no current use.	M	█	12/30/2021	7/29/2021	
█	Rodents	7/28/2021	Found expired artifical tears, tissue glue. All items were discarded at time of inspections	M	█	12/30/2021	7/28/2021	
█	Small Animals	9/27/2021	Expired drugs were also found in the █ laboratory. These were taken and disposed of during the inspection.	M	█ █	3/22/2021	9/27/2021	
█	Rodents	11/18/2021	Found expired Ketofen and Lidocaine. Segregated and labeled " expired not for animal use".	M	█	5/30/2022	12/16/2021	

MSU IACUC Membership Roster

MSU IACUC Membership November 2021

IACUC Chairperson [REDACTED]			
Name of Member/ Code*	Degree/ Credentials	Position Title	PHS Policy Membership Requirements***
Danielle Ferguson	DVM, MS	Interim Attending Veterinarian	Veterinarian, Scientist
8	M.Div	Minister	Non-scientist, Nonaffiliated
9	Ph.D	Associate Professor / Food Science & Human Nutrition	Scientist
13	MAB	Industry President	Nonaffiliated
19	LVT, LATg, CPIA	IACUC Administrator / Research Liaison	Scientist
33	Ph.D	Associate Professor / Pathobiology & Diagnostic Investigation	Scientist
35	DVM	Clinical Veterinarian (Alternate)	Scientist
40	[REDACTED] Ph.D,	Assistant Professor/Farm Veterinarian	Scientist
41	[REDACTED]	Librarian	Scientist
43	BS	Research Assistant / Animal Science	Scientist
44	Ph.D	Professor / Translational Science & Molecular Medicine	Scientist
46	Ph.D	Associate Professor / Neuroscience	Scientist
47	Ph.D	Professor / Animal Science	Scientist
48	BS, MS	Community Member	Scientist, Nonaffiliated
50	Ph.D	Associate Professor / Animal Science	Scientist
51	Ph.D	Assistant Professor / Radiology	Scientist
52	Ph.D	Assistant Professor / Fisheries & Wildlife	Scientist
53	Ph.D	Senior Extension Specialist-Small Ruminants / Large Animal Clinical Sciences	Scientist
54	BS, DVM, [REDACTED]	Associate Professor / Small Animal Clinical Sciences	Scientist
E1	MS	Animal Handler Safety Officer / EHS (alternate)	Scientist

*** [PHS Policy](#) Membership Requirements:

Veterinarian veterinarian with training or experience in laboratory animal science and medicine or in the use of the species at the institution, who has direct or delegated program authority and responsibility for activities involving animals at the institution.

Scientist practicing scientist experienced in research involving animals.

Nonscientist member whose primary concerns are in a nonscientific area (for example, ethicist, lawyer, member of the clergy).

Nonaffiliated individual who is not affiliated with the institution in any way other than as a member of the IACUC, and is not a member of the immediate family of a person who is affiliated with the institution. This member is expected to represent general community interests in the proper care and use of animals and should not be a laboratory animal user. A consulting veterinarian may not be considered nonaffiliated.

MICHIGAN STATE UNIVERSITY
CURRENTLY APPROVED EXCEPTIONS

PROTOCOL / AUF #	SPECIES	Exception to...					EXCEPTION
		AWA	Guide	Ag Guide	MSU Guide	N/A	
201800151	Mouse		x				Approved an exception for feed. Growth restriction is associated with increased risk of cardiovascular disease. To induce postnatal under nutrition there are two methods that are widely used 1) feed dams a low protein diet or 2) altering the litter size to increase competition during nursing. Option 1, low protein diet induces less stress and results in more continuity between pub weight, which is why we have selected it.
201800173	Rat		x		x		Approved an exception for feed. In order to motivate rats to respond for the appetitive reinforcers subjects are typically food or water restricted. I have published extensively using these food and fluid restriction procedures (e.g., Johnson et al., 2009, J. Neurosci, Vol. 29:696-704; Sherwood et al., 2012, E J Neurosci, Vol. 36(8): 3126-3133) and report no significantly adverse reactions to the animal as a result of their implementation. In the extremely unlikely event that an animal is unable to be maintained or struggles with this restriction, they will be subsequently removed from the study and provided with unlimited access to food or fluid prior to being euthanized.
202000012	Mouse		x				Approved an exception for feed. The dams in this experiment will be randomly assigned to two specialized diets that have been extensively utilized previously by our lab in the "Postnatal Growth-Restriction" procedure. Specifically, one diet is a normal protein (NP) feed, consisting of 20% protein that meets the nutritional needs of the animal. The other diet is a low protein (LP) feed, that is isocaloric to the NP feed, but consists of only 8% protein (difference in calories made up by carbohydrates). Dams will be placed on these diets two weeks prior to breeding, and will continue on this diet until pups are weaned.
202000026	Mouse		x				Approved an exception for feed. Two weeks prior to breeding, dams will be randomly assigned to two specialized diets, made by Research Diets. One feed will be our control, consisting of adequate protein content (20% protein). The other diet will be considered our "low protein" feed, which is an isocaloric feed to the control diet, and consist of an 8% protein (the low protein feed is isocaloric through an increase in carbohydrates).
201900370	Mouse		x			x	Approved an exception for feed: Experiment 7c. The animals will be fed ad libitum (AL) before the IF is initiated at the onset of diabetes. The db/m and db/db mice will be each divided in two subgroups, AL feeding (control) and IF, wherein the animals will be fasted for 24 h every other day for 6 months, beginning at night. Dysregulation of normal pattern of circadian food intake has been recently shown to contribute to diabetes induced vascular damage type 2 diabetic mice. Normalizing the food intake pattern by limiting the hours when food is available through alternative day fasting intermittent fasting (IF) protocol was previously shown by other and us to improve metabolic health, increase the rate of survival and prevent complications in the diabetic animals. The BKS.Cg-Dock7m +/- Leprdb/J strain is chosen for this experiment because these diabetic (homozygous) mice can withstand, and improve their metabolic profile and overall health due to the prolonged fast. Although prolonged fasting cannot be used for all strains of mice, for this strain prolonged fasting is well tolerated and beneficial to animal health.

MICHIGAN STATE UNIVERSITY
CURRENTLY APPROVED EXCEPTIONS

PROTOCOL / AUF #	SPECIES	Exception to...					EXCEPTION
		AWA	Guide	Ag Guide	MSU Guide	N/A	
201900111	Mouse		x		x		<p>Approved an exception for water, bedding, sanitation/waste disposal, and feed. Water will be restricted for a maximum of 24 hours to increase the osmolarity of the plasma in mice.</p> <p>Germ-free mice lack all microorganisms (as determined within the limitations of the detection methods available) and will be housed in tightly controlled and monitored isolators to prevent contamination. All materials used with germ free mice will be double bagged for autoclaving with thermal chemical indicator tips with each item being autoclaved to verify sterility.</p> <p>Water restriction increases serum osmolarity to the level of a moderately controlled diabetic patients. This approach has been previously reported in the literature to induce hyperosmotic conditions in mice (Chen et al., J. Clin. Invest. 119:1647-1658, 2009; Morris et al., Hypertension 33:482-6, 1999; FEBS Letters 584 (2010) 2883-2890). We have successfully done these studies but need to repeat the study for rigor.</p> <p>Due to a lack of microbiota germ free mice can be easily contaminated (no longer germ free) if rigid handling and husbandry protocols are not adhered to.</p>
202000218	Mouse		x		x		<p>Approved an exception for lighting and water. Mice involved in our Acute awake in vivo electrophysiological experiments will be housed on a reverse light-cycle (12:12). In addition, some mice designated for these experiments will be placed on a water restriction (See Procedure Water restriction). Reverse Light Cycle: Our current in vivo recording studies require tests in alert, behaving mice because the neural circuits we are interested in studying, ultimately, need to be probed during behaviors that engage the circuits. The room will be set on a reverse light-cycle (12:12) with light-dark transitions occurring at 10 AM and 10 PM. Water restriction: (see Procedure for Water restriction for details and further justification) Our current in vivo recording studies require tests in alert, behaving mice because the neural circuits we are interested in studying, ultimately, need to be probed during behaviors that engage the circuits. Thus, the purpose of using water restriction for our experiments is to aid acclimation to the recording setup and motivate mice to perform simple behaviors while recording electrophysiological signals in the brain.</p>
202000312	Rat		x		x		<p>Approved an exception for space requirements. Cable connections for long term stimulation are not compatible with standard rat caging.</p>
202100007	Mouse		x				<p>Approved an exception for lighting and cage changes. Mice will be maintained the minimal amount of time in constant darkness possible. When the phenotype of the transgenic mouse studied is strong, 3-4 weeks in constant darkness is sufficient to conclude the study. However, in some cases it takes longer to reveal a phenotype, in some cases as long as 7-10 weeks. To obtain meaning full circadian wheel running data, it is important the mice are disturbed as little as possible. Cage changes can entrain wheel-running activity, and thus interfere with the study. When mice are singly housed with the running wheel, cage changes will be done every 21 days. If the cages become excessively dirtied or animal health issues arise, the CAR veterinary staff have the authority to request an earlier cage change date.</p>

MICHIGAN STATE UNIVERSITY
CURRENTLY APPROVED EXCEPTIONS

PROTOCOL / AUF #	SPECIES	Exception to...					EXCEPTION
		AWA	Guide	Ag Guide	MSU Guide	N/A	
202100219	Mouse		x				Approved an exception for temperature/humidity. Experiments will be performed at either standard room temperature or thermoneutral temperature (28 - 30C). Our research examines the effects of environmental contaminants and drugs on metabolic disease. Several studies have reported that thermoneutral conditions better model human metabolic disease, particularly cardiovascular and non-alcoholic fatty liver diseases. Experiments in thermoneutral conditions will test those hypotheses for the investigation of chemical and drug exposures.
202100230	Mouse		x				Approved an exception for feed. We will use custom research diets to induce postnatal growth restriction caused by under nutrition. Growth restriction is associated with increased risk of cardiovascular disease. To induce postnatal under nutrition there are two methods that are widely used 1) feed dams a low protein diet or 2) altering the litter size to increase competition during nursing. Option 1, low protein diet induces less stress and results in more continuity between pub weight, which is why we have selected it.
202100221	Mouse		x		x		100% food and water restriction following infection with Enterobacter species. The mouse pups will not go through the typical acclimation phase. Instead, they will be inoculated immediately upon arrival to the lab
201900163	Mouse		x				Approved an exception for temperature/humidity. Experiments will be performed at 28-30 C, within the mouse TNZ. Recent data in the laboratory animal literature indicates that housing mice at "standard" room temperatures of 20-22 C versus within their TNZ at 28-30 C may have profound impacts on their physiology, drug metabolism, and use as models of human diseases. The metabolic activation in mice housed at 20-22 C has also been demonstrated to have impacts on their reproductive success and behavior (huddling with conspecifics, quality of nest building).
202000212			x		x		The study of mouse behavior (wheel running activity) in constant darkness is the only way to reveal the endogenous free-running period of the suprachiasmatic nucleus, the master pacemaker of the body.