SEMIANNUAL REPORT

ANIMAL CARE AND USE
PROGRAM REVIEW AND FACILITY INSPECTION
OF THE

_____NIEHS_____

April 2020

Section A – Site Visits & Program Review

1) Inspections of the ***IC name*** animal facilities (AF), satellite holding facilities (SF), USDA-defined study areas for regulated species (SA) and areas where any surgical manipulations (Surg) are performed (as applicable) were conducted as indicated below:

Location	Type	Date	ACUC Members
Redacted by agreement	AF, Surg	2/14/2020 and 2/18-21/2020	Cook, Redacted by agreement
	Surg	3/16/2019	Redacted by agreement
	SF	3/12/2020	
	AF	8/28/2019	

2) Visits by at least one member of the ACUC to all remaining areas where animal activities were performed were conducted. These visits occurred during the previous six months and findings and corrective actions are described in this or the previous semiannual report.

3) The following document(s) was/were used as the basis for review of the animal care and use program:

	Document/Resource:
X	Guide for the Care & Use of Laboratory Animals, 8th Edition (Guide)
X	AAALAC Program Description
X	OACU "Animal Program Semiannual Assessment Checklist" (1 page summary)
X	OACU/OLAW "Semiannual Program Review & Facility Inspection Checklist" (24 pages)
X	NIEHS Semiannual walk through summary
X	NIEHS Animal Facility Checksheet
X	NIEHS Laboratory Inspection Log
X	NIEHS Standard Operating Procedures and Guidelines

4) The program review was conducted in the following manner:

	Program Review Process
	Full committee member review for *ALL* of the review, i.e. the documents/resources listed in A3) are included in the meeting packet and reviewed at a fully convened meeting
X	Full committee and subcommittee review, i.e. the documents/resources listed in A3) are assigned to various members who review their parts/sections and then they discuss their reviews with the full committee for a final review/approval
	Designated member review, i.e. the documents/resources listed in A3) are assigned to various members who review their parts/sections and then report back to the full committee the results of their designated review

	Other, please describe:

Section B – Regulatory Compliance:
Except as noted in Section F below, the facilities and program are in full compliance with the Public Health Service Policy, the Animal Welfare Act Regulations and the Guide, which were used as the basis for this evaluation.

Section C – Program Changes:
The following administrative and procedural changes have occurred since the program was last evaluated:

1) Administrative/Procedural Changes:
a) The NIEHS SOPs for the NIEHS Animal Health Surveillance Programs, Animal Pathogen Detection: Immediate Room Quarantine Procedures, C129B-Importation and Care of Rodents from outside sources, and Screening of Biological Materials for Contaminating Microorganisms were presented, discussed, and approved by the ACUC on 11/21/2019.
b) The NIEHS Guidelines for Resolving Non-Compliance Issues, NIEHS Guideline for the Use of Controlled Substances, NIEHS Animal Care and Use Committee Guidelines, NIEHS Euthanasia Methods for Rodent Fetuses and Neonates, Isoflurane Euthanasia, Decapitation Procedures for Mice and Rats, Hypothermia of Neonates, Whole Body Perfusion, Liver Perfusion, Jugular Cannulation, Neonatal Intracranial Surgery (PND 0-3), Artificial Insemination, Tissue Biopsy for Genotyping, Fostering Mouse Pups, Vaginal Wash, Hormone Preparation (PMSG and HCG) and Administration, Embryo Transfer (non-surgical), Embryo Transfer (surgical), Genetically Engineered Mouse Breeding Colonies, NIEHS Guidelines for the Estimation of Animal Numbers for ASPs with breeding, Tissue Specific Gene Disruption breeding scheme, Tm1-flox-null colonies breeding scheme, LoxP-flanked Marker Removal breeding scheme, Flox to null colony breeding scheme, In vivo Removal of FRT-flanked Positive Selection Marker, NIEHS Guideline on Determining Standard Nomenclature for Tg and KO animals, Caliper/Xenogen Spectrum In Vivo Imaging System (IVIS), NIEHS Guideline for Endpoints in Solid Tumor Studies Set Up and Operation of the Kent Scientific CODA Blood Pressure System were presented, discussed, and approved by the ACUC 12/11/2019.
c) On January 23, 2020 the ACUC discussed, reviewed, and approved SOPs for Clinical Barbering, Blood Pressure Monitoring, Cesium Irradiation of Animals, Dermatitis Endpoints, Isoflurane Anesthesia System, Oropharyngeal Aspiration, Blood Collection: Retro-orbital Sinus (Rat), Blood Collection: Retro-orbital Vein (Mouse), Tracheal intubation/Instillation (Rat), Intra-ocular Pressure Measurement, Oral Gavage, Voltmeter Membrane Resistance Reading for Estrous Cycle Tracking (Rat), Bruker Body Mass Analyzer, ECGenie Non-invasive ECG, Faxitron UltraFocus Imaging/DEXA, Cardiac Ultrasound (Anesthetized), Cardiac Ultrasound (Conscious), Controlled Substances Guideline - CAF , and Ordering Customized Antibodies. In addition, the committee reviewed and approved the NIEHS Facility Disaster Plan.
d) The ACUC added language to the ASP form to clarify the human or animal disease and pathology that is being studied February 27, 2020.
e) The ACUC guideline was modified to allow the head of a core laboratory to stay in the room during discussions of protocols on which they are the PI or a participant so that these persons, considered experts, can answers questions of the committee. These members must leave prior to final deliberation and voting. The committee voted unanimously to approve this change on February 27, 2020.

f) SOPs for Phenomaster, blood collection methods, IP Glucose tolerance test, Insulin tolerance test, the Labmaster, and injection methods were reviewed and approved February 27, 2020.
g) Modifications to the NIEHS Facility Disaster Plan were presented, discussed, and approved at the March 26, 2020 meeting. Changes included identification of husbandry procedures that are outside of the Guide standards in response to significantly decreased staffing during pandemic situations and the addition of COVID-19 social distancing, facility, and sanitation procedures.
h) SOPs for Animal Biosafety Level (ABSL) I and II Procedures, Animal Ordering in eSirius, Cameras and Video Recorders in the Animal Facility, Carcass and Cage Disposal, Care and Selection of Mice and Rats for Timed Breeding, Environmental Enrichment for Mice and Rats, Guideline for Controlled Substances – Redacted by agreement Guideline for Controlled Substances – CAF, Pest Control Program (CMB), Providing Dietary Mash for Supportive Care of Rodents, Social Housing Procedures for Mice and Rats, Tail Tattooing for Mice and Rats, Thin Client and Laptop Computer Use in Animal Rooms, Use of Procedure/Necropsy Rooms, Clinical Animal Health Reporting – Weekend, Clinical Animal Health Reporting – Workweek, Mouse Craniotomy, Electrode, or Optical Probe Insertion, Mouse Craniotomy for Injection, and Mouse Craniotomy for GRIN Lens Implantation were reviewed, discussed and approved March 26, 2020.
i) On April 23, 2020 the ACUC reviewed SOPs for Blood Pressure, Decidualization via the vagina, Adrenalectomy, Terminal Bile Duct Cannulation, Bile Collection, Caesarab Section Rederivation, Carotid Cannulation, Carotid Ligation, Castration, Castration of Neonates, Cecal Ligation Puncture, and ECG implant.

2) Key Personnel Changes - ACUC Chair, ACUC Attending Vet, APD, or Program Manager:

Role (ACUC Chair, ACUC AV, IC APD, or IC Animal Program Manager)	**Name**	**Action** (joined or departed)
NA		

3) Animal Facility/Area Changes:

Facility Type (AF/SF)	**Location**	**Action** (opened, closed, under renovation, etc.)
NA		

Section D – Guide Departures & USDA Exceptions:
Departures from the standards of the *Guide* and exceptions to the USDA *Animal Welfare Act Regulations,* which have been approved by the Animal Care and Use Committee, include the following:

1. Departures from the Guide:

Guide Departures	***Guide Departure Citation (page #)***	***Justification** (scientific, veterinary, or animal welfare)*

Rodents housed on wire flooring	Guide page 51	Protocols approved include a scientific justification for the use of metabolism cages if housed on perforated stainless-steel flooring for greater than 24 hours. These animals are acclimated to the chambers and are monitored by the CMB Veterinary Medicine Section. No problems have been observed. Currently there are five approved studies for housing mice and rats in metabolism cages for >24 hours. A protocol is approved with a scientific justification for a maternal bedding restriction study involving the housing of mouse dams and pups for a period of 1 week during the timeframe of pups being between postnatal day (P) 2 and P17 in a standard cage with fine mesh and a nesting square to induce stress in the mothers and pups. A protocol is approved with a scientific justification for a 24-48 hour fast on perforated flooring to minimize coprophagy.
Ambient Housing temperature not in accordance with Guide recommendations	Guide page 43	A protocol is approved with a scientific justification for housing mice at 4C for a maximum of 16 hours in order to study specific gene expression involved in energy metabolism. These animals have been monitored by the CMB Veterinary Medicine Section and no problems have been observed. A protocol is approved with scientific justification for housing mice at 4C for 4 weeks to study the effects of cold exposure on metabolism. Animals are monitored daily and then more frequently as core body temperature begins to drop. The CMB Veterinary Medicine Section will actively monitor the animals with the lab. A protocol is approved with a scientific justification for housing mice at 4C for 5 - 8 hrs without enrichment to study the effect of cold exposure on

		metabolism and energy expenditure. The CMB Veterinary Medicine Section will actively monitor the animals with the lab.
Prolonged Restraint	Guide page 29-30	One protocol is approved for prolonged restraint for a period of two hours repeated five consecutive days without acclimation to the restraint system to induce stress-related feeding behavior. The study participants continuously monitor mice during the restraint protocol. If mice fail to acclimate within fifteen minutes as determined by intense persistent struggling behavior, the restraint procedure will be terminated and the animal removed from the protocol. One protocol is approved for prolonged restraint for a period of three hours repeated thirty consecutive days to restrict vertical activity to induce stress. The animal is still able to move forward and backward. Intense distress is not expected because horizontal movement is not impeded. Study participants continuously monitor mice during the vertical restriction protocol.

2. Exceptions to the AWAR:

Species	***# Animals Affected (this Period)***	***9CFR title/section***	***Description and Rationale***
NA			

Section E – Previous Deficiencies & Plans:
The committee validated that the plans and schedules for deficiencies noted during the previous NIEHS program review, and facilities and laboratory inspections were achieved within the time intervals projected on the previous semiannual report.

Section F – Current Deficiencies & Plans:
Deficiencies found *over the past 6 months* during NIEHS program review, facility inspections, and laboratory inspections, are as follows:

	Deficiency	[1]M/S	Location	Correction Plan	Responsible Party	Scheduled Completion Date (mm/dd/yy)	[2]Status: C/P
1	Expired Buprenorphine	M	Redacted by agreement	PI was not using the expired	Investigator	3/12/20	C

				Buprenorphine and it was removed immediately.			
2	Expired Xylazine	M	Redacted by agreement	PI was not using the expired Xylazine and it was returned to the CSO.	Investigator	3/12/20	C
3	Controlled Substances were not appropriately documented in the controlled substance log and small amounts were drawn up in syringes that unlabeled or labeled as having been drawn up >30 days before the inspection and did not include the CS expiration date.	M	Redacted by agreement	The CSO met with the lab to discuss the controlled substances procedures. The custodian, teleworking during the pandemic is unable to draw up controlled substances so the CSO is providing the lab with the needed drugs.	Investigator/CSO	3/24/20	C
4	Controlled Substance Log documentation was incomplete.	M	Redacted by agreement	The CSO was contacted and provided the lab with a copy of the controlled substance SOP and provided training on the maintenance of the controlled substance log.	Investigator/CSO	3/13/20	C

[1]M=minor; S=significant **[2]C=corrected; P=pending**

Section G – Reportable Events:

PHS Policy (i.e. OLAW) reportable events that occurred in the last 6 months or that are still awaiting final disposition are as follows: **[X] None**

Section H – Shared & Central Facilities:

This semiannual report also encompasses review and oversight of animals and animal activities which were present or occurred in shared or central facilities. Deficiencies were noted and transmitted directly to the facility, and if necessary, to the responsible Animal Care and Use Committee. These reviews were conducted as indicated below:

This section does not apply to this IC.

Section I – Minority Report

There is not a minority report filed with this semiannual report.

NIEHS ACUC Member Signatures:

Donald N. Cook -SR1 Digitally signed by Donald N. Cook -SR1 Date: 2020.04.29 15:07:43 -04'00'

Don Cook, PhD
Chair, ACUC

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Redacted by agreement

Kathy Laber, DVM

Redacted by agreement

Redacted by agreement

Redacted by agreement

(Revised - 09/2019)

Semiannual Report Attachment 3
Supplemental Information
Fall 2019

Instructions: Submit the following information with your Fall 2019 Semiannual Report as a separate file called IC SI F19.

NOTE: *Guide* Exceptions (IC REP Fall 2019, section D): a reminder that a new column was added in the spring 2019 cycle asking for the *Guide* citation for Exceptions (*Guide* chapter, section, and page number).

1. **Number of approved Animal Study Proposals (ASPs) as of 31 Oct 2019:**

Provide the total number of active/approved ASPs as of the 31 October 2019 cutoff date.
133 total active ASPs

2. **Performance standards:**

Provide a description of ACUC approved performance standards. For additional information and examples, see the "Guide Departures & Performance Standards" document developed by OACU.

i. Solid bottom cages in all mouse ventilated cage racks are changed using NIEHS established and ACUC approved performance standards. The maximum interval between changes is two weeks. Intracage ammonia, relative humidity, and air changes were evaluated at various cage densities and cage changing frequencies using the current ventilated caging system at NIEHS. Ammonia and relative humidity levels were below levels reported in current literature to cause nasal epithelial degeneration. Care is taken to ensure the environment is dry and spot changing is completed if a cage is identified during the daily health observations by the husbandry staff (Guide page 70)

ii. Mouse cages in four semi-rigid gnotobiotic isolators receive a weekly bedding change but are not sanitized at weekly intervals because the CRASF or germ-free mice lack urease-positive bacteria. Monthly (germ-free) and quarterly (defined-flora) evaluations of gnotobiotic mice by QAL confirms microbial status. Identification of any bacteria in the germ-free or urease-producing bacteria in the defined-flora isolators indicates contamination. Once detected, these isolators are broken down, re-sterilized and restocked. (Guide page 70)

iii. Social housing will be considered the default method of housing mice and rats. Due to the aggressive nature exhibited by BALB/c, FVB, and SJL strains, as documented in current literature, male mice on these backgrounds are singly housed upon arrival. Because C57BL/6 male mice (including genetically engineered mice on a C57BL/6 background) are generally non-siblings at or near the age of puberty at the time experimental studies are initiated, individual housing is recommended to prevent fighting. Male mice are housed individually when designated for breeding. These male mice are housed alone in their own cage for several days prior to breeding. In the absence of other animals, additional enrichment is provided, as appropriate. (Guide page 51)

NATIONAL INSTITUTES OF HEALTH
Facilities and Animal Species Inventory Table
Assurance Number: A-4149-01

IC Name: National Institute of Environmental Health Sciences

Semiannual Report Submission Date: April 30, 2020

Spring Program Review Date(s):	3/26/20					

Fall Program Review Date(s):						

Bldg/Area/Rm	Facility Insp. Date(s) Spring / Fall		AF/SF; Gross Sq. Ft.	Species Housed			Average Daily Inventory		
Redacted by agreement	3/12, 3/13, 3/16, 3/19		72,250	1 Mice	2 Rats	3	1 35,481	2 233	3
				4	5	6	4	5	6
	2/21/20		953	1 Mice	2	3	1 125	2	3
				4	5	6	4	5	6
	3/12/20		197.5	1 Mice	2	3	1 0	2	3
				4	5	6	4	5	6
				1	2	3	1	2	3
				4	5	6	4	5	6
				1	2	3	1	2	3
				4	5	6	4	5	6

Semiannual Report Attachment 3
Supplemental Information
Spring 2020

Instructions: Submit the following information with your Spring 2020 Semiannual Report as a separate file called IC SI S20.

Performance Standards:
Provide a description of ACUC-approved performance standards. For additional information and examples, see the "Guide Departures & Performance Standards" document developed by OACU.

i. Solid bottom cages in all mouse ventilated cage racks are changed using NIEHS established and ACUC approved performance standards. The maximum interval between changes is two weeks. Intracage ammonia, relative humidity, and air changes were evaluated at various cage densities and cage changing frequencies using the current ventilated caging system at NIEHS. Ammonia and relative humidity levels were below levels reported in current literature to cause nasal epithelial degeneration. Care is taken to ensure the environment is dry and spot changing is completed if a cage is identified during the daily health observations by the husbandry staff (Guide page 70)

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Veterinary Verification & Consultation:
If your IC has a VVC policy, please include a copy with your semiannual report submission.

The NIEHS VVC process is described on page 6 and 7 of the attached NIEHS Animal Care and Use Committee Guideline.

Animal Adoption:
If applicable, please provide the number of animals adopted from your IC by species.
If your IC has an adoption policy, please include a copy with your semiannual report submission.

NA

Member Name	Degree/Credentials	Position Title	PHS Policy Membership Role	New Member
Don Cook	PhD	Principal Investigator	Chair	☐
Kathy Laber	DVM, DACLAM	Animal Program Director	Attending Veterinarian	☐
Redacted by agreement				☐
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Don Cook, PhD

Redacted by agreement

Attending Vet Phone - Redacted by