

**MINUTES OF MEETING**  
**NIEHS ANIMAL CARE AND USE COMMITTEE**  
**April 23, 2020; 1:00 pm**  
**Virtual Meeting through Zoom**

Members Present: Dr. Don Cook (Chair), [Redacted by agreement]  
[Redacted by agreement] Dr. Kathy Laber, [Redacted by agreement]  
[Redacted by agreement]  
[Redacted by agreement] (15/15 members present; quorum assured)

Also Present: [Redacted by agreement]  
[Redacted by agreement]  
[Redacted by agreement]

The minutes of the March 26, 2020 ACUC meeting were approved.

ARAC Meeting: Dr. Cook summarized the April 22, 2020 ARAC meeting. The main topic covered was building plans for the new Center for Disease Research on the main NIH campus. The next ARAC meeting is scheduled for May 27, 2020.

Monthly VMS Report: [Redacted by agreement] reported that there are no active studies that require VMS monitoring.

Semi-Annual Report: [Redacted by agreement] presented the Spring 2020 semi-annual report. The report will be submitted to the NIH OACU by April 30, 2020.

COVID-19 update: [Redacted by agreement] reported that NIH animal resource representatives from each IC and division are meeting daily to discuss the ongoing COVID-19 Pandemic and its effect on NIH function.

World Week for Animals in laboratories 2020: The ACUC typically reviews the NIEHS Animal Rights Contingency Plan in April, but it is now included in the NIEHS Disaster Plan which was last reviewed and approved by the ACUC in March, 2020. No animal rights activities were announced in the RTP area. PETA held a drive-by demonstration in front of NIH and at the homes of NIH leadership.

NIEHS Standard Operating Procedures: [Redacted by agreement] presented the SOPs listed below and included in the meeting packet to the ACUC. Members were given an opportunity to ask questions and discuss each SOP. All of the SOPs were unanimously approved.

1. Blood Pressure – CODA system
2. Decidualization via the vagina (non-surgical; 4/2020)
3. Adrenalectomy – mouse
4. Adrenalectomy – rat
5. Bile Duct Cannulation (terminal) – rat
6. Bile Collection – mouse
7. Caesarian Section Rederivation (terminal) – mouse
8. Carotid Cannulation
9. Carotid Ligation – rat
10. Castration

11. Castration of neonates
12. Cecal Ligation Puncture – mouse
13. ECG Implant – mouse

Distributed to ACUC

Email:

None

Distributed to NIEHS ASP Participants

Email:

None

Each of the following proposals and amendments was reviewed for all issues covered in the instructions to investigators including rationale for work, appropriateness of animal model and animal numbers used, method of euthanasia, surgical and post-operative care and issues related to pain and distress of animals. All actions, unless noted otherwise, reflect a unanimous action on the part of committee members present and no minority viewpoints were expressed during the ACUC deliberations.

## NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - PROPOSED FOR FULL COMMITTEE REVIEW

Project Number, Branch	Principal Investigator	Project Title	ACUC Reviewer
Redacted by agreement	Redacted by agreement	<b>(Approved)</b> Use of Transgenic and Knockout Mice to Study Zfp36 (TTP), Zfp36l1 (TIS11B), Zfp36l2 (TIS11D), and Zfp36l3; <u>(Add More Animals:</u> Add 550 CD-1 mice; <u>Change in Animal Procedures:</u> Add cesarean section rederivation; Add tamoxifen administration).	Redacted by agreement
(b)(5)			
Redacted by agreement	Redacted by agreement	<b>(Approved with one abstention)</b> Epigenetic Changes in Mouse Intestine in Response to Diet; <u>(Add More Animals:</u> Add 24 C57BL/6 mice; <u>Change in Animal Procedures:</u> Add 4C cold room exposure [vs. 17C or 12C]).	Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Approved)</b> Pilot Study of Sex Differences in Neurobehavioral Tests. <b>(Renewal)</b> <div>Redacted by agreement</div> listed as the PI of the study, left the meeting during deliberations and voting and did not contribute to a quorum.	Redacted by agreement

## NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - REVIEWED BY DESIGNATED MEMBER REVIEW

Project Number, Branch	Principal Investigator	Project Title	Approval Date Reviewer
Redacted by agreement	Redacted by agreement	Chemokine and Toll-like Receptor Adaptor Function in Pulmonary Inflammation; ( <u>Add More Animals</u> : Add 100 C57BL/6J mice; <u>Change in Animal Procedures</u> : Increase dose and frequency of Poly (i:c) to up to 50ug daily for up to 7 days for new study [previously approved for 0.5ug administered twice]; increase OVA dose to 100 ug given via OPA).	April 20, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Genetic Manipulation of Hippocampal CA2 Neurons; ( <u>Add More Animals</u> : Add Grik4-cre;cFOS-GFP/tTA, GAD-GFP; Grik4-cre, and GIN;Grik4-cre mouse lines and 1536 total animals for breeding and colony maintenance).	April 20, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Renewal)</b> Role of Cholinergic Signaling in Brain Function: Use of Transgenic Mouse Models and Viral Constructs.	April 22, 2020 Redacted by agreement

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – REVIEWED BY VETERINARY VERIFICATION AND CONSULTATION

Project Number, Branch	Principal Investigator	Project Title	Approval Date/ Vet Reviewer
Redacted by agreement	Redacted by agreement	Chemokine and Toll-like Receptor Adaptor Function in Pulmonary Inflammation; ( <u>Change in Animal Procedures</u> : Change urethane dose to 2-2.5g/kg to reflect change in FlexiVent SOP).	March 27, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Role of GWAS Candidate Genes in Lung Function; ( <u>Change in Animal Procedures</u> : Change urethane dose to 2-2.5g/kg to reflect updated FlexiVent SOP).	March 30, 2020 Redacted by agreement

Redacted by  
agreement

Redacted by  
agreement

The Role of LC3-associated  
Phagocytosis in Autoimmune and  
Inflammatory Disorders; (Change in  
Animal Procedures: Change urethane  
dose to 2-2.5g/kg to reflect updated  
FlexiVent SOP).

March 27, 2020

Redacted by  
agreement

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – MINOR ADMINISTRATIVE CHANGES

Project Number, Branch	Principal Investigator	Project Title	Approval Date
Redacted by agreement	Redacted by agreement	Breeding protocol to produce Conditional Glucocorticoid Receptor Knock-out mice; ( <u>Add a New Participant</u> : Redacted by agreement)	April 10, 2020
Redacted by agreement	Redacted by agreement	Conditional Glucocorticoid Receptor Knockout in Murine B Cells; ( <u>Add a New Participant</u> : Redacted by agreement)	April 10, 2020

## ANNUAL REVIEW OF ANIMAL USE ACTIVITIES – Reviewed by Designated Member Review by

Redacted by agreement

Project Number, Branch	Principal Investigator	Project Title
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None

## SUBMISSIONS PREVIOUSLY REVIEWED AND NOT APPROVED – REQUIRING MODIFICATIONS TO SECURE APPROVAL

Project Number, Branch	Principal Investigator	Project Title	NA Date Reviewer
Redacted by agreement	Redacted by agreement	The Role of Lipids in Pulmonary Innate Immunity; ( <u>Add More Animals</u> : Add 768 mice from approved strains [Column E]; <u>Change in Animal Procedures</u> : Add MOG, IFA, Mycobacterium tuberculosis, and Pertussis Toxin injections for experimental autoimmune encephalomyelitis [EAE] procedure).	March 26, 2020 Redacted by agreement

**MINUTES OF MEETING**  
**NIEHS ANIMAL CARE AND USE COMMITTEE**  
**May 28, 2020; 1:00 pm**  
**Virtual Meeting through Zoom**

Members Present: Dr. Don Cook (Chair), [Redacted by agreement]  
[Redacted by agreement] Dr. Kathy Laber, [Redacted by agreement]  
[Redacted by agreement]  
(14/15 members present; quorum assured)

Also Present: [Redacted by agreement]  
[Redacted by agreement]

Absent: [Redacted by agreement]

The minutes of the April 23, 2020 ACUC meeting were approved.

ARAC Meeting: Dr. Cook summarized the May 27, 2020 ARAC meeting. The meeting was focused on COVID-19's impact on the NIH animal program. [Redacted by agreement] lead a discussion on the framework for returning to the workplace. NIH will not use thermal imaging to monitor individuals returning to work as it does not reliably identify COVID-19 cases. Staff will receive five cloth masks to wear on campus. Masks will be required while on an NIH site or campus. This requirement will be enforced by the Scientific Directors, supervisors, and staff members reporting violations to a hotline. The next ARAC meeting is scheduled for June 24, 2020.

Monthly VMS Report: [Redacted by agreement] reported that VMS is actively monitoring two studies and adverse clinical signs have been reported. Two memos to the record have been filed.

- [Redacted by agreement] 05-23, IIDL. VMS monitored high dose poly I:C OVA study. No adverse clinical signs were observed.
- [Redacted by agreement] 06-18, IIDL. VMS remotely monitored a Listeria study taking place in the Conventional Animal Facility. One mouse was removed due to reaching the weight loss endpoint, but no other clinical signs were reported.

COVID-19 update: [Redacted by agreement] shared a morale-boosting video created by the animal care staff. [Redacted by agreement] presented a summary of the NIEHS COVID-19 response report that she had given to the NIH ART. Challenges included implementation of social/physical distancing and the need for increased sanitation of common areas. NIEHS has not had any reported COVID-19 cases, so husbandry staff shortages have not been an issue, to date. CMB implemented staggered shifts for animal care staff to limit the number of employees in locker and break rooms. Husbandry schedules have been altered and although the number of staff in the animal facility at any one time has been reduced, there have been no changes in the quality of husbandry care. Investigators have been supportive during the pandemic by halting non-essential studies when possible and maintaining breeding colony sizes at maintenance levels. All changes in husbandry, PPE, and staffing during the pandemic has been reviewed and approved by the ACUC in the NIEHS disaster plan. Dr. Laber indicated that CMB is working on guidance for PIs on re-entry into more active animal work in the vivarium.

NIEHS Standard Operating Procedures: Redacted by agreement presented the SOPs listed below and included in the meeting packet to the ACUC. Members were given an opportunity to ask questions and discuss each SOP. All of the SOPs were unanimously approved.

1. Behavior (Neurobehavioral Core) – Operant Touch Screen Tasks
2. Behavior – Avoidance Learning
3. Behavior – Forced Swim
4. Behavior – Functional Observational Battery (FOB)
5. Behavior – Hotplate
6. Behavior – Morris Water Maze
7. Behavior – Radial Arm Maze
8. Behavior – Running Wheel
9. Behavior – Startle Reflex
10. Behavior – Tail Flick
11. Clinical – Chlorhexidine
12. Procedure – Faxitron Ultrafocus Imaging
13. Surgery – Craniotomy: EEG/EMG Implant (mouse)
14. Surgery – Craniotomy: Electrode/Optical Probe
15. Surgery – Craniotomy: IC Injection
16. Surgery – Craniotomy: GRIN lens
17. Surgery – Intraductal Injection in Mammary Gland

Distributed to ACUC

Email:  
None

Distributed to NIEHS ASP Participants

Email:  
None

Each of the following proposals and amendments was reviewed for all issues covered in the instructions to investigators including rationale for work, appropriateness of animal model and animal numbers used, method of euthanasia, surgical and post-operative care and issues related to pain and distress of animals. All actions, unless noted otherwise, reflect a unanimous action on the part of committee members present and no minority viewpoints were expressed during the ACUC deliberations.

#### NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - PROPOSED FOR FULL COMMITTEE REVIEW

Project Number, Branch	Principal Investigator	Project Title	ACUC Reviewer
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move 360 Mop3-/- mice to Col. E; Change in Animal Procedures: Add circadian entrainment study with mice housed in total darkness and telemetry implant surgeries; Add xenograph study with intraductal injections into the mammary gland and tumor monitoring in conjunction with ovex/castr surgery and hormone injections).

Redacted by agreement	Redacted by agreement	( <b>Approved</b> ) Metabolism and Disposition Studies of Ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoate (GenX); ( <u>Add More Animals</u> : Add carotid cannulated rats from the vendor and move 100 rats to Col. D; <u>Change in Animal Procedures</u> : Add in situ brain perfusion as a route for approved compounds; Add decap under anesthesia as a euthanasia method).	Redacted by agreement
Redacted by agreement	Redacted by agreement	( <b>Approved</b> ) Development of Cholinergic Neurons in the Brain; ( <u>Add More Animals</u> : Add 386 Vgat-flox x Chat-cre/ROSAtdT mice for approved Col. E procedures and 144 Vgat-flox x Chat-cre mice; <u>Change in Animal Procedures</u> : Add transfer of mice to the UNC Behavior Core for phenotyping).	Redacted by agreement
Redacted by agreement	Redacted by agreement	( <b>Approved</b> ) <small>Redacted by agreement</small> Reproductive Biology Investigations; ( <u>Add More Animals</u> : Add 1344 C57BL/6J mice; <u>Change in Animal Procedures</u> : Add the following drugs for new experiment: Wnk463, W11, propylene glycol, HPC, and pluronic F68).	Redacted by agreement

## NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - REVIEWED BY DESIGNATED MEMBER REVIEW

Project Number, Branch	Principal Investigator	Project Title	Approval Date Reviewer
Redacted by agreement	Redacted by agreement	Regulation of Nicotinic Receptor Synaptic Transmission in the Rodent Brain; ( <u>Add More Animals</u> : Add the following new strains and a total of 664 mice for breeding and colony maintenance: CAG-Cas9-EGFP, ChAT-Cre x CAG-Cas9-EGFP, RiboTag, and vGAT-flox/ChAT-cre x RiboTag).	May 12, 2020 Redacted by agreement

Redacted by agreement	Redacted by agreement	<b>(Renewal)</b> Investigation of mechanisms underlying Bleomycin-induced Pulmonary Fibrosis.	May 28, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Breeding of Genetically Engineered Mice for Experimental Analysis; ( <u>Add More Animals</u> : Adding 120 P2X7 KO mice for breeding and colony maintenance).	May 20, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Mechanism of Fertilization; ( <u>Add More Animals</u> : Add 96 Ai14 x Zp3-creM, 332 Zp3 x CreM, 6 Ai14, and 22 C57BL/6J mice for breeding and colony maintenance).	May 6, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Mechanism of Fertilization; ( <u>Add More Animals</u> : Add 2 Wnk1flox and 272 Wnk1flox x Zp3-cre mice for breeding and colony maintenance).	May 14, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Investigation of Mechanisms Underlying Respiratory Virus-induced Airway Disorders. <b>(Renewal)</b>	May 13, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Redacted by agreement Breeding Protocol; ( <u>Add More Animals</u> : Add the following new strains and a total of 1,152 mice for breeding and colony maintenance: Ddx4-cre, Ddx4-creWnk1flox, PPP2R1Aflox, and PRCrePPPR1Aflox).	May 1, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Mechanistic Study of the Impact of Environmental Factors on Neurological Disorders; ( <u>Change in Animal Procedures</u> : Update monitoring of PD mouse model strain based on PI experience. Mice will be monitored once/week beginning at 24 weeks [previously 15 weeks] and twice per week beginning at 25 weeks [previously 20 weeks]).	April 27, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Mechanistic Study of the Impact of Environmental Factors on Neurological Disorders; ( <u>Add More Animals</u> : Add 270 A2A/Tfam mice for approved procedures).	May 6, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	MBD3 Mutant Mouse Generation. <b>(Renewal)</b>	May 19, 2020 Redacted by agreement

Redacted by agreement	Redacted by agreement	Terminal Nucleotidyl-Transferases (TENTs) Animal Protocol; ( <u>Add More Animals</u> : Add 504 Ddx4-cre/ERT2 Tut4 Del Tut7-flox and 504 Cre-Ert2 Tut4 Del Tut7-flox mice for breeding and approved procedures).	May 19, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Nrf2 (Nfe2l2) Knock-In Mouse Breeding Colonies. <b>(New Proposal)</b>	May 13, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Knockout Core Auxiliary Protocol; ( <u>Add More Animals</u> : Add 808 R26-hACE2 and 808 hsACE2 mice for breeding and colony maintenance).	April 28, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Previously NOT APPROVED, Required Modifications to Secure Approval)</b> Dynamics of Gene Expression Heterogeneity. <b>(New Proposal)</b>	April 27, 2020 Redacted by agreement

## NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - REVIEWED BY EXPEDITED REVIEW

Project Number, Branch	Principal Investigator	Project Title	Approval Date Reviewer
Redacted by agreement	Redacted by agreement	Chemokine and Toll-like Receptor Adaptor Function in Pulmonary Inflammation; ( <u>Add More Animals</u> : Add 378 C57BL/6J mice; <u>Change in Animal Procedures</u> : Add the following new compounds for COVID-19 experiment: MRS5980, MRS7154, MRS4669, MRS4654, A-438079, and A-740003).	May 8, 2020 Redacted by agreement

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – REVIEWED BY VETERINARY VERIFICATION AND CONSULTATION

Project Number, Branch	Principal Investigator	Project Title	Approval Date/ Vet Reviewer
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None

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – MINOR ADMINISTRATIVE CHANGES

Project Number, Branch	Principal Investigator	Project Title	Approval Date
Redacted by agreement	Redacted by agreement	Breeding protocol to produce Conditional Glucocorticoid Receptor Knock-out mice; (Add a New Participant: Redacted by agreement)	May 14, 2020
Redacted by agreement	Redacted by agreement	Conditional Glucocorticoid Receptor Knock-out in the Heart; (Add a New Participant: Redacted by agreement)	May 14, 2020
Redacted by agreement	Redacted by agreement	Conditional Glucocorticoid Receptor Knock-out in Mouse Liver; (Add a New Participant: Redacted by agreement)	May 14, 2020

## SUBMISSIONS PREVIOUSLY REVIEWED AND NOT APPROVED – REQUIRES MODIFICATIONS TO SECURE APPROVAL

Project Number, Branch	Principal Investigator	Project Title	NA Date Reviewer
(b)(5)			

## ANNUAL REVIEW OF ANIMAL USE ACTIVITIES – Reviewed by Designated Member Review by

Redacted by agreement			
Project Number, Branch	Principal Investigator	Project Title	
Redacted by agreement	Redacted by agreement	Regulation of Nicotinic Receptor Synaptic Transmission in the Rodent Brain. (Continue with changes – see amendment)	

Redacted by agreement

Redacted by agreement

Metabolism and Disposition Studies of Brominated Components of a Commercial Flame Retardant. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Mechanistic Study of the Impact of Environmental Factors on Neurological Disorders (breeding protocol). **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

In Vivo Study of the Role of Acetylcholine in Learning and Memory. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Metabolism and Disposition Studies of Ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoate (GenX). **(Continue with changes – see amendment)**

**MINUTES OF MEETING**  
**NIEHS ANIMAL CARE AND USE COMMITTEE**  
**June 25, 2020; 1:00 pm**  
**Virtual Meeting through Zoom**

Members Present:	Dr. Don Cook (Chair),	Redacted by agreement
	Redacted by agreement	Dr. Kathy Laber,
	Redacted by agreement	Redacted by agreement
Redacted by agreement	(15/15 members present; quorum assured)	
Also Present:	Redacted by agreement	
	Redacted by agreement	

The minutes of the May 28, 2020 ACUC meeting were approved.

ARAC Meeting: Dr. Laber summarized the June 24, 2020 ARAC Meeting. The NIH main campus has postponed their AAALAC site visit to 2021 due to the COVID-19 pandemic and NIEHS has followed suit. The guideline for Significant Changes to Animal Study Proposals was reviewed and approved. The next ARAC meeting is scheduled for July 22, 2020.

Monthly VMS Report: No active studies that require VMS monitoring are ongoing.

COVID-19 update: Dr. Laber referred the committee to Redacted by agreement All Hands meeting for the latest COVID-19 updates.

Plans for Group A re-entry to Animal Facility: Dr. Laber summarized the NIEHS SOP for re-entry into the workplace. Animal care staff will continue to work in shifts to ensure social distancing and sanitization in common use areas. The current schedule can be maintained with the addition of ~1500 more cages, so PIs have been asked to carefully plan breeding and experiments accordingly. Upon entering an animal room, staff should remove their face covering don a mask provided by CMB in the vivarium. There will be a limit of 2 people per animal and procedure room. Surgeries will be scheduled by VMS.

NIEHS Standard Operating Procedures: Redacted by agreement presented the SOPs listed below and included in the meeting packet to the ACUC. Members were given an opportunity to ask questions and discuss each SOP. All of the SOPs were unanimously approved.

1. Surgery – Anesthesia Record Checksheet
2. Surgery – Anesthesia Record Keeping
3. Surgery – Anesthesia Surgery Report
4. Surgery – Embryo Transfer
5. Surgery – Hepatectomy (mouse)
6. Surgery – Hepatic Injection (mouse)
7. Surgery – Hypophysectomy (mouse)
8. Surgery – Implant under Kidney Capsule (mouse)
9. Surgery – IP Pump/Transmitter implant
10. Surgery – Mammary Gland Clearing and Transplantation
11. Surgery – Ovarian Transplantation (mouse)
12. Surgery – Ovariectomy

- 13. Surgery – Ovariectomy of Neonates
- 14. Surgery – Uterine Injection into Lumen

Distributed to ACUC

Email:

None

Distributed to NIEHS ASP Participants

Email:

None

Each of the following proposals and amendments was reviewed for all issues covered in the instructions to investigators including rationale for work, appropriateness of animal model and animal numbers used, method of euthanasia, surgical and post-operative care and issues related to pain and distress of animals. All actions, unless noted otherwise, reflect a unanimous action on the part of committee members present and no minority viewpoints were expressed during the ACUC deliberations.

### NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - PROPOSED FOR FULL COMMITTEE REVIEW

Project Number, Branch	Principal Investigator	Project Title	ACUC Reviewer
Redacted by agreement	Redacted by agreement	<b>(Approved)</b> Sirtuin and NAD+ Metabolism in Tumorigenesis; ( <u>Add More Animals</u> : Add 144 C57BL/6NTac and 144 C57BL/6NTac (GF) mice; <u>Change in Animal Procedures</u> : Administer nicotinamide via drinking water (previously approved via feed); Add immune check point inhibitors Anti-pd1 and Anti-ctla4 antibodies given IP in conjunction with antibiotics, nicotinamide, and SQ injections of cancer cells previously approved).	Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Approved)</b> Role of SIRT1 in Intestinal Stress Response and Inflammation; ( <u>Add More Animals</u> : Add 192 conGR-VillinCre mice (all Col. E); <u>Change in Animal Procedures</u> : Add IP injections of Chlodronate or control liposomes in conjunction with DSS-treated drinking water administration previously approved).	Redacted by agreement
Redacted by agreement	Redacted by agreement	Evaluation of Hippocampal Neural Progenitor Cells and Altered Neuroimmune Regulation as Influenced by Arsenic Exposure. <b>(No Longer Active)</b>	

# NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - REVIEWED BY DESIGNATED MEMBER REVIEW

Project Number, Branch	Principal Investigator	Project Title	Approval Date Reviewer
Redacted by agreement	Redacted by agreement	Generation, Initial Characterization and Maintenance of P450 and Soluble Epoxide Hydrolase Transgenic Mice. <b>(Renewal)</b>	June 11, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Breeding of Genetically Engineered Mice for Experimental Analysis; ( <u>Add More Animals</u> : Add 240 Trv1 cre and 240 ST2fx-Trv1 Cre mice for breeding and colony maintenance).	June 18, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Necropsy and Tissue Collection for DNTP and NIEHS Investigators. <b>(Renewal)</b>	June 19, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Glucocorticoid Receptor Phosphorylation Site Knock-in Mice. <b>(Renewal)</b>	June 16, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Conditional Glucocorticoid Receptor Knockout in Murine B Cells; ( <u>Add More Animals</u> : 144 GR fl/fl and 144 GR fl/fl x Mb1-cre mice; <u>Change in Animal Procedures</u> : Add RO blood collection; Add pristane injections [PI has previous experience]).	June 18, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Role of SIRT1 in Intestinal Stress Response and Inflammation; ( <u>Add More Animals</u> : Add 192 conT1B6-Defa6cre mice [Column C]; <u>Change in Animals Procedures</u> : Add IVIS imaging; the following new compounds [PI has previous experience] in combination with approved procedures: IgG2b control antibody, enrofloxacin, anti-PD-L1 antibody, and MC-38).	June 4, 2020 Redacted by agreement

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – REVIEWED BY VETERINARY VERIFICATION AND CONSULTATION

Project Number, Branch	Principal Investigator	Project Title	Approval Date/ Vet Reviewer
None			

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – MINOR ADMINISTRATIVE CHANGES

Project Number, Branch	Principal Investigator	Project Title	Approval Date
Redacted by agreement	Redacted by agreement	Activity-dependent regulation of neuronal gene expression; (Add a New Participant: Redacted by agreement)	June 17, 2020
Redacted by agreement	Redacted by agreement	Analysis of Hormone Signaling in Mice Deficient in Histone Subtypes and Histone Modifying Enzymes; (Add a New Participant: Redacted by agreement)	May 29, 2020
Redacted by agreement	Redacted by agreement	Functional Assessment of Hippocampal Area CA2; (Add a New Participant: Add Redacted by agreement)	June 17, 2020
Redacted by agreement	Redacted by agreement	Genetic Manipulation of Hippocampal CA2 Neurons; (Add a New Participant: Add Redacted by agreement)	June 17, 2020
Redacted by agreement	Redacted by agreement	In Vivo Electrophysiological and Behavioral Analyses of CA2 Function; (Add a New Participant: Add Redacted by agreement)	June 17, 2020
Redacted by agreement	Redacted by agreement	Embryonic Stem Cell and Induced Pluripotent Stem Cell Evaluation; (Add a New Participant: Add Redacted by agreement)	May 29, 2020
Redacted by agreement	Redacted by agreement	Regulation and Function of Mineralocorticoid Receptors in Hippocampal CA2 Neurons; (Add a New Participant: Add Redacted by agreement)	June 17, 2020

Redacted by agreement	Redacted by agreement	Breeding and Maintenance Protocol for Studies of LC3-associated Phagocytosis as a Critical Regulator of Inflammation; (Add a New Participant: Add Redacted by agreement)	June 12, 2020
Redacted by agreement	Redacted by agreement	Tissue and Sample Harvest for the Study of LC3-associated Phagocytosis; (Add a New Participant: Add Redacted by agreement)	June 12, 2020
Redacted by agreement	Redacted by agreement	The Role of LC3-associated Phagocytosis in the Development of Diabetes Mellitus; (Add a New Participant: Add Redacted by agreement)	June 12, 2020
Redacted by agreement	Redacted by agreement	The Role of LC3-associated Phagocytosis in Autoimmune and Inflammatory Disorders; (Add a New Participant: Add Redacted by agreement)	June 12, 2020
Redacted by agreement	Redacted by agreement	The Role of LC3-associated Phagocytosis in Arthritis and Colitis Models; (Add a New Participant: Add Redacted by agreement)	June 12, 2020
Redacted by agreement	Redacted by agreement	The Role of LC3-associated Phagocytosis in Pathogen and Immunization Models; (Add a New Participant: Add Redacted by agreement)	June 12, 2020
Redacted by agreement	Redacted by agreement	The Role of DNASE1L3 in Tumorigenesis; (Add a New Participant: Add Redacted by agreement)	June 4, 2020

#### ANNUAL REVIEW OF ANIMAL USE ACTIVITIES – Reviewed by Designated Member Review by

Redacted by agreement

Project Number, Branch	Principal Investigator	Project Title
Redacted by agreement	Redacted by agreement	Characterization of COX Mice. (Continue with no changes)
Redacted by agreement	Redacted by agreement	Mechanistic Study of the Impact of Environmental Factors on Neurological Disorders. (Continue with no changes)

**SUBMISSIONS PREVIOUSLY REVIEWED AND NOT APPROVED – REQUIRES MODIFICATIONS TO SECURE APPROVAL**

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<b>Project Number, Branch</b>	<b>Principal Investigator</b>	<b>Project Title</b>	<b>NA Date Reviewer</b>
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**MINUTES OF MEETING**  
**NIEHS ANIMAL CARE AND USE COMMITTEE**  
**July 23, 2020; 1:00 pm**  
**Virtual Meeting through Zoom**

Members Present: Dr. Don Cook (Chair), [Redacted by agreement]  
[Redacted by agreement] Dr. Kathy Laber, [Redacted by agreement]  
[Redacted by agreement]  
(14/15 members present; quorum assured)

Also Present: [Redacted by agreement]  
[Redacted by agreement]

Absent: [Redacted by agreement]

The minutes of the June 25, 2020 ACUC meeting were approved.

ARAC Meeting: Dr. Cook summarized the June 22, 2020 ARAC meeting. COVID-19 was discussed with nothing new to report. Dr. Cook reminded the committee that as group A returns to NIEHS campus, researchers should be conservative in their efforts to expand breeding colonies within the animal facility as studies resume. A notification was sent to the ASP participants and Dr. Zeldin is supportive of limited colony expansion at this time. The NIH main campus has postponed their AAALAC site visit to 2021 due to the COVID-19 pandemic and NIEHS has followed suit. NIH was site visited by OLAW early in 2020. Several recommendations were made by OLAW that NIH has already begun to address. NIEHS will make changes, as needed, in response to the OLAW recommendations. The August ARAC meeting is scheduled for August 26, 2020.

Monthly VMS Report: [Redacted by agreement] reported that VMS is monitoring two studies with no adverse events to report. One MTR was finalized.

- [Redacted by agreement] The clodronate study was monitored. There were no unexpected adverse side effects noted. The MTR was finalized and filed on the CMB server.

COVID-19 update: Beginning at the end of March, the ventilated cage change schedule was extended from 14 days to up to 28 days as stated and approved in the NIEHS disaster plan. Cubicles and cages on study continued to be changed per ASP. CMB leadership and module supervisors have been performing rounds to make sure the standard of animal care was maintained and the rounds have been documented weekly. There has been no evidence that animal welfare has been adversely impacted and CMB requested a return to the standard oversight of husbandry. The committee voted to resume standard oversight.

NIEHS Standard Operating Procedures: [Redacted by agreement] presented the SOPs listed below and included in the meeting packet to the ACUC. Members were given an opportunity to ask questions and discuss each SOP. All of the SOPs were unanimously approved.

1. Heat Pad Operations
2. Carbon Dioxide Euthanasia of Rodents
3. Tail Vein Injection
4. Blood Pressure Monitor Implantation
5. Partial Hepatectomy in Rats

6. Jugular Cutdown in Mice
7. Jugular Cutdown in Rats
8. Laparotomy
9. Splenectomy
10. Subcutaneous Implantation of Tumors
11. Transverse Aortic Constriction in Mice
12. Tumor Debulking
13. Vagotomy in Mice
14. Vasectomy in Mice

Distributed to ACUC

Email:

None

Distributed to NIEHS ASP Participants

Email:

Animal Research Guidance for Group A Re-entry; July 14, 2020 (Laber)

ESS and Transfer Requests; July 22, 2020 Redacted by agreement

Each of the following proposals and amendments was reviewed for all issues covered in the instructions to investigators including rationale for work, appropriateness of animal model and animal numbers used, method of euthanasia, surgical and post-operative care and issues related to pain and distress of animals. All actions, unless noted otherwise, reflect a unanimous action on the part of committee members present and no minority viewpoints were expressed during the ACUC deliberations.

## NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - PROPOSED FOR FULL COMMITTEE REVIEW

Project Number, Branch	Principal Investigator	Project Title	ACUC Reviewer
<span style="border: 1px solid black; padding: 2px;">Redacted by agreement</span>	<span style="border: 1px solid black; padding: 2px;">Redacted by agreement</span>	<b>(Approved)</b> Role of SIRT1, Stress hormone, and Metabolism in Intestinal Stress Response and Inflammation. <b>(Renewal)</b>	<span style="border: 1px solid black; padding: 2px;">Redacted by agreement</span>
<span style="border: 1px solid black; padding: 2px;">Redacted by agreement</span>	<span style="border: 1px solid black; padding: 2px;">Redacted by agreement</span>	<b>(Approved)</b> Metabolic and Epigenetic Regulation of Cancer and Stem Cell Differentiation. <b>(Renewal)</b>	<span style="border: 1px solid black; padding: 2px;">Redacted by agreement</span>
<span style="border: 1px solid black; padding: 2px;">Redacted by agreement</span>	<span style="border: 1px solid black; padding: 2px;">Redacted by agreement</span>	<b>(Approved)</b> Conditional Glucocorticoid Receptor Knock-out in Mouse Liver; <u>Add More Animals</u> : Add 32 vendor-adrenalectomized C57BL/6 mice; <u>Change in Animal Procedures</u> : Add an experiment with Eplerenone-treated diet, Dexamethasone-treated water, Faxitron DEXA scans,	<span style="border: 1px solid black; padding: 2px;">Redacted by agreement</span>

submandibular blood collection, and blood pressure measurements).

(b)(5)

## NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - REVIEWED BY DESIGNATED MEMBER REVIEW

Project Number, Branch	Principal Investigator	Project Title	Approval Date Reviewer
Redacted by agreement	Redacted by agreement	The Role of Eicosanoids in Established Murine Models of Lung Disease. <b>(Renewal)</b>	July 14, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Chemokine and Toll-like Receptor Adaptor Function in Pulmonary Inflammation; ( <u>Add More Animals</u> : Add 120 P2X7 KO [B6.129P2-P2rx7 <sup>tm1Gab</sup> /J] mice for approved procedures).	July 10, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Breeding Protocol for Studies of the Role of Cholesterol Trafficking in Lung Inflammation; ( <u>Add More Animals</u> : Ms4a3, ROSA-tdTomato9, Ms4a3-TdT, Irgm1-TdT and Ms4a3-TdT-Irgm1 mouse lines and 744 total animals for breeding and colony maintenance).	July 2, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Breeding colony for transgenic experimental strains; ( <u>Add More Animals</u> : Add 4 C57BL/6J and 388 PDGFRA-EGFP mice for breeding and colony maintenance).	July 20, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Mechanism of Fertilization; ( <u>Add More Animals</u> : Add 32 C57BL/6J, 238 Crl:CD1(ICR), and 598 Pmca1 x Zp3-cre mice; <u>Change in Animal Procedures</u> : Add high fat diet challenge; Add paw tattooing to identify animals prior to weaning).	July 8, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Identifying the Process of Reproductive Organ Formation. <b>(Renewal)</b>	July 21, 2020 Redacted by agreement

Redacted by agreement	Redacted by agreement	Genetic Manipulation of Hippocampal CA2 Neurons; ( <u>Add More Animals</u> : Add 512 Ar fl/fl and 512 Am2-cre(8); Ar fl/fl mice for breeding and approved procedures).	July 16, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Regulation and Function of Mineralocorticoid Receptors in Hippocampal CA2 Neurons; ( <u>Add More Animals</u> : Add 3465 Am2-GFP mice [Column C and D]; <u>Change in Animal Procedures</u> : Add cross-fostering in combination with approved procedures).	July 23, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Physiological Function of Glis3 Protein. <b>(Renewal)</b>	July 22, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Role of Hyaluronan associated proteins in tobacco-induced inflammation. <b>(Renewal)</b>	July 21, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	The Role of DNASE1L3 in Tumorigenesis; ( <u>Add More Animals</u> : Add 128 Dnase1L3, 20 OT-I, and 20 OT-II mice; <u>Change in Animal Procedures</u> : Combine previously approved MC-38 and doxorubicin injections).	July 10, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Nrf2 (Nfe2l2) Knock-In Mouse Breeding Colonies; ( <u>Other Changes</u> : Replace approved strain 129S6 with 129S1).	July 1, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Previously Not Approved)</b> Dynamics of Gene Expression Heterogeneity; ( <u>Add More Animals</u> : Add 720 NSG CD34FL mice and move 360 Mop3 <sup>-/-</sup> mice to Col. E; <u>Change in Animal Procedures</u> : Add circadian entrainment study with mice ovariectomized or castrated, implanted with telemetry devices and housed in total darkness; Add xenograph study with intraductal injections into the mammary gland and tumor monitoring in conjunction with ovariectomy surgery and hormone injections).	July 8, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Environmental Modulators of SARS-CoV-2 Cell Entry Factor Expression. <b>(New Proposal)</b>	July 10, 2020 Redacted by agreement

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – REVIEWED BY VETERINARY VERIFICATION AND CONSULTATION

Project Number, Branch	Principal Investigator	Project Title	Approval Date/ Vet Reviewer
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None

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – MINOR ADMINISTRATIVE CHANGES

Project Number, Branch	Principal Investigator	Project Title	Approval Date
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Redacted by agreement	Redacted by agreement	Use of Transgenic and Knockout Mice to Study Zfp36 (TTP), Zfp36l1 (TIS11B), Zfp36l2 (TIS11D), and Zfp36l3; (Add a New Participant: Add Redacted by agreement)	July 13, 2020
Redacted by agreement	Redacted by agreement	Role of SIRT1 in Intestinal Stress Response and Inflammation; (Add a New Participant: Add Redacted by agreement)	June 26, 2020
Redacted by agreement	Redacted by agreement	Breeding and Maintenance Protocol for Studies of LC3-associated Phagocytosis as a Critical Regulator of Inflammation; (Add a New Participant: Add Redacted by agreement)	July 22, 2020
Redacted by agreement	Redacted by agreement	Tissue and Sample Harvest for the Study of LC3-associated phagocytosis; (Add a New Participant: Add Redacted by agreement)	July 22, 2020
Redacted by agreement	Redacted by agreement	The Role of LC3-associated Phagocytosis in the Development of Diabetes Mellitus; (Add a New Participant: Add Redacted by agreement)	July 22, 2020
Redacted by agreement	Redacted by agreement	The Role of LC3-associated Phagocytosis in Autoimmune and Inflammatory Disorders; (Add a New Participant: Add Redacted by agreement)	July 22, 2020
Redacted by agreement	Redacted by agreement	The Role of LC3-associated Phagocytosis in Arthritis and Colitis Models; (Add a New Participant: Add Redacted by agreement)	July 22, 2020

Redacted by  
agreement

Redacted by  
agreement

The Role of LC3-associated Phagocytosis July 22, 2020  
in Pathogen and Immunization Models;  
(Add a New Participant: Add

Redacted by  
agreement

Redacted by  
agreement

**ANNUAL REVIEW OF ANIMAL USE ACTIVITIES – Reviewed by Designated Member Review by**  
Redacted by agreement

Project Number, Branch	Principal Investigator	Project Title
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Redacted by  
agreement

Redacted by  
agreement

Inter-alpha-trypsin Inhibitor in Wound Healing and  
Angiogenesis after Injury. **(Continue with no changes)**

Redacted by agreement

Redacted by  
agreement

Breeding Colony for Transgenic Experimental Strains.  
**(Continue with no changes)**

Redacted by agreement

Redacted by  
agreement

Tlr5 in Inflammatory and Fibrotic Disease. **(Continue with  
no changes)**

**SUBMISSIONS PREVIOUSLY REVIEWED AND NOT APPROVED – REQUIRING  
MODIFICATIONS TO SECURE APPROVAL**

Project Number, Branch	Principal Investigator	Project Title	NA Date Reviewer
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(b)(5)

**MINUTES OF MEETING**  
**NIEHS ANIMAL CARE AND USE COMMITTEE**  
**August 27, 2020; 1:00 pm**  
**Virtual Meeting through Zoom**

Members Present: Dr. Don Cook (Chair), [Redacted by agreement]  
[Redacted by agreement] Dr. Kathy Laber, [Redacted by agreement]  
[Redacted by agreement] (13/15 members present; quorum assured)

Also Present: [Redacted by agreement]  
[Redacted by agreement]

Absent: [Redacted by agreement]

The minutes of the July 23, 2020 ACUC meeting were approved.

ARAC Meeting: The August ARAC meeting was cancelled. The next ARAC meeting is scheduled for September 23, 2020.

Monthly VMS Report: No active studies that require VMS monitoring are ongoing.

COVID-19 update: Dr. Laber reminded the committee the need to continue to wear face masks while on campus.

NIEHS Standard Operating Procedures: [Redacted by agreement] presented the SOPs listed below and included in the meeting packet to the ACUC. Members were given an opportunity to ask questions and discuss each SOP. All of the SOPs were unanimously approved.

1. Mouse Bleeding Times (Terminal)
2. Subcutaneous Implantation of Mini-Pumps or pellets requiring an incision

LPS Pilot Study: [Redacted by agreement] presented the findings from a pilot study performed by VMS under ASP 2016-0007 to examine the clinical signs associated with LPS dosing. The study was completed at the request of the ACUC as multiple investigators at NIEHS use LPS models and the approved ASPs have different endpoints and monitoring, which have been topics of discussion at previous ACUC meetings. The study aim was to determine the ideal dosing time and monitoring schedule based on appearance of clinical signs. The study, which consisted of 20 mice with 5 animals per sex per dose, was performed in mid-August using 5mg/kg and 10mg/kg doses. Mice were implanted with subcutaneous temperature transponders prior to the study. VMS dosed the mice between 10am and noon and the mice were monitored every 2 hours for 48 hours and euthanized at the 48 hour endpoint. Body temperature and weight were monitored and the mice were scored for hunched posture, reduced activity, and unkempt coat. Criteria for euthanasia included 20% weight loss and moribundity. Two animals were euthanized for hypothermia and morbidity. VMS found the critical time period for clinical signs to be between 14/16 hours and 20 hours post injection. Based on the findings of this pilot study, VMS recommends that monitoring initiate at a minimum every 2 hours 12-24 hours post dosing, and then every 2-4 hours thereafter based on strain. They also recommend supportive care in the form of extra enrichment, food on the floor, mash, and group housing for mice to help

regulate body temperature as their body temperature decreases. Those animals that cannot be group housed should be monitored more frequently to assess decreases body temperature. [Redacted by agreement] emphasized the need for accurate dosing, by determining doses based upon the individual weights of each animal and dosing LPS that has been thoroughly sonicated. The committee requested an LPS guideline to be written to standardize care and monitoring for future LPS studies.

Fall 2020 Site Visit Alternative: [Redacted by agreement] reported to the committee that OLAW has offered the following flexibilities in the conduct of semiannual animal facility inspections:

- The timing of facility inspections may extend 30 days beyond the six-month interval from the last review if there is no forward drift of the date from year to year.
- The IACUC has discretion to determine the best means of conducting the facility inspections. This includes using any qualified individual as *ad hoc* consultants. For areas housing non-USDA regulated species, the IACUC may use as few as one qualified individual to conduct the inspections. The IACUC still remains responsible for the evaluation and report to the Institutional Official.

The ACUC voted to have [Redacted by agreement] and [Redacted by agreement] perform the animal room and animal use area inspections and to allow labs to be inspected by CMB veterinarians and [Redacted by agreement]  
[Redacted by agreement]

Distributed to ACUC

Email:

None

Distributed to NIEHS ASP Participants

Email:

None

Each of the following proposals and amendments was reviewed for all issues covered in the instructions to investigators including rationale for work, appropriateness of animal model and animal numbers used, method of euthanasia, surgical and post-operative care and issues related to pain and distress of animals. All actions, unless noted otherwise, reflect a unanimous action on the part of committee members present and no minority viewpoints were expressed during the ACUC deliberations.

## NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - PROPOSED FOR FULL COMMITTEE REVIEW

Project Number, Branch	Principal Investigator	Project Title	ACUC Reviewer
[Redacted by agreement]	[Redacted by agreement]	(Approved) Glucocorticoid Receptor Isoforms Knock-In Mice. (Renewal)	[Redacted by agreement]

Redacted by agreement	Redacted by agreement	<b>(Approved)</b> Sirtuins and NAD metabolism in Aging and Age-associated Diseases. <b>(Renewal)</b>	Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Approved)</b> In Vivo Study of the Role of Acetylcholine in Learning and Memory; ( <u>Add More Animals</u> : Add 40 C57BL/6, 40 Gad2-cre, and 200 Wfs1-Tg3-creERT2 mice [column E]; <u>Change in Animal Procedures</u> : Add the following new compounds administered IC or IP: ethosuximide, Z944, NC 55-0396, and ZD7288; Add 4 new AAV variations).	Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Approved)</b> Tumorigenesis of Immortalized Human Endometrial Epithelial Cells (ht-UtEEC) in Nude Mice. <b>(New Proposal)</b>	Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Approved)</b> The Effects of Continuous Cadmium Exposure on Cancer Progression in Uterine Fibroid (ht-UtLM) Cells. <b>(New Proposal)</b>	Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Approved)</b> The Role of Lipids in Pulmonary Innate Immunity; ( <u>Add More Animals</u> : Add 216 C57BL/6J mice, 108 Flot2-OT-1, 108 Flot2-Pmel-1, 324 OT-1, and 324 Pmel-1 mice; <u>Change in Animal Procedures</u> : Add murine T cells, OVA-B6F10 tumor cells, and Lentiviral shRNA-treated T cells for new experiment).	Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Approved)</b> The Role of Inter-alpha-trypsin Inhibitor in Wound Healing and Angiogenesis after Injury; ( <u>Add More Animals</u> : Add 960 TLR4 mice for approved acute Bleomycin study [column C, D, and E]). Redacted by agreement listed as a participant on the study, left the meeting during deliberations and voting and did not contribute to a quorum.	Redacted by agreement
Redacted by agreement	Redacted by agreement	Breeding Protocols for Generating Primary Brain Neuron-Glial Cultures. <b>(No Longer Active)</b>	
Redacted by agreement	Redacted by agreement	Do Physiologic Parameters of Mice Vary with Caging Type? <b>(No Longer Active)</b>	

## NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - REVIEWED BY DESIGNATED MEMBER REVIEW

Project Number, Branch	Principal Investigator	Project Title	Approval Date Reviewer
Redacted by agreement	Redacted by agreement	Role of Eicosanoids in the Cardiovascular System. <b>(Renewal)</b>	Aug. 12, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Chemokine and Toll-like Receptor Adaptor Function in Pulmonary Inflammation; ( <u>Add More Animals</u> : Add 240 uPar [B6.129P2-Plaur <sup>tm1Jld</sup> /J] mice for approved procedures).	July 29, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Redacted by agreement Breeding Protocol; ( <u>Add More Animals</u> : Add 288 Ddx4creERT2-mTmG mice for breeding and colony maintenance).	July 30, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Redacted by agreement Breeding Protocol; ( <u>Add More Animals</u> : Add 288 LtflCrexCTCF-flox and 288 LtflCrexZmiz1-flox mice for breeding and colony maintenance).	Aug. 11, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	<b>(Previously Not Approved)</b> Molecular analysis of dopamine neuron loss in mouse models of Parkinson's Disease. <b>(Renewal)</b>	July 29, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Maintenance and Generation of Mouse Models to Investigate Mechanisms Underlying Microglia Dysfunction in Neurodegeneration; ( <u>Change in Animal Procedures</u> : Add blanket breeding protocol).	Aug. 25, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Dynamics of Gene Expression Heterogeneity; ( <u>Change in Animal Procedures</u> : Add 20 Ex3aERKO mice for approved procedures).	Aug. 5, 2020 Redacted by agreement

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – REVIEWED BY VETERINARY VERIFICATION AND CONSULTATION

Project Number, Branch	Principal Investigator	Project Title	Approval Date/ Vet Reviewer
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Redacted by  
agreement

Redacted by  
agreement

Role of P450 Products in Vascular Inflammation; (Change in Animal Procedures: Add feces collection as a justification for single housing female as well as male cohorts for approved colitis studies).

July 29, 2020

Redacted by agreement

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – MINOR ADMINISTRATIVE CHANGES

Project Number, Branch	Principal Investigator	Project Title	Approval Date
Redacted by agreement	Redacted by agreement	Chemokine and Toll-like Receptor Adaptor Function in Pulmonary Inflammation; ( <u>Add a New Participant</u> : Add Redacted by agreement)	August 25, 2020
Redacted by agreement	Redacted by agreement	Necropsy and Tissue Collection for DNTP and NIEHS Investigators; ( <u>Add a New Participant</u> : Add Redacted by agreement)	August 4, 2020
Redacted by agreement	Redacted by agreement	Pilot Study of Sex Differences in Neurobehavioral Tests; ( <u>Add a New Participant</u> : Add Redacted by agreement)	August 14, 2020
Redacted by agreement	Redacted by agreement	Metabolism and Disposition Studies of Ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoate (GenX); ( <u>Add a New Participant</u> : Add Redacted by agreement)	July 28, 2020
Redacted by agreement	Redacted by agreement	Maintenance and Generation of Mouse Models to Investigate Mechanisms Underlying Microglia Dysfunction in Neurodegeneration; ( <u>Add a New Participant</u> : Add Redacted by agreement)	July 23, 2020
Redacted by agreement	Redacted by agreement	Maintenance and Generation of Mouse Models to Investigate Mechanisms Underlying Microglia Dysfunction in Neurodegeneration; ( <u>Add a New Participant</u> : Add Redacted by agreement)	Aug. 17, 2020

**ANNUAL REVIEW OF ANIMAL USE ACTIVITIES – Reviewed by Designated Member Review by**  
**Redacted by agreement**

Project Number, Branch	Principal Investigator	Project Title
Redacted by agreement	Redacted by agreement	Generation and Maintenance of Transgenic, Estrogen Receptor Transgenics and Estrogen Receptor Knockout Breeding Colonies. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Regulation of Nicotinic Receptor Synaptic Transmission in the Rodent Brain. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	The Use of Knockout Mice to Study MARCKS. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Use of Transgenic and Knockout Mice to Study Zfp36 (TTP), Zfp36l1 (TIS11B), Zfp36l2 (TIS11D), and Zfp36l3. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Activity-Dependent Regulation of Neuronal Gene Expression. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Characterization of COX Mice. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Chemokine and Toll-like Receptor Adaptor Function in Pulmonary Inflammation. <b>(Continue with changes – see amendment)</b>
Redacted by agreement	Redacted by agreement	Physiological Function of Glis Proteins. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Study of the Function of the Nuclear ROR Receptors. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	The Role of Inter-alpha-trypsin Inhibitor in Wound Healing and Angiogenesis After Injury. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Breeding Colony for Transgenic Experimental Strains. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Receptor Mechanisms in Hormone-Sensitive Cells Derived from STIM and Orai1 Mouse Models. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Functional Assessment of Hippocampal Area CA2. <b>(Continue with no changes)</b>
Redacted by agreement	Redacted by agreement	Physiological function of JAZF1/TIP27. <b>(Continue with no changes)</b>

Redacted by agreement

Redacted by agreement

Physiological Function of RORa. **(Continue with no changes)**.

Redacted by agreement

Redacted by agreement

Genetic Manipulation of Hippocampal CA2 Neurons. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

In Vivo Electrophysiological and Behavioral Analyses of CA2 Function. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Breeding protocol for GWAS Candidate Genes in Lung Function. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

GWAS Candidate Genes in Lung Function. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Metabolism and Disposition Studies of Brominated Components of a Commercial Flame Retardant. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Mechanistic Study of the Impact of Environmental Factors on Neurological Disorders (breeding protocol). **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Tissue and Sample Harvest of the Study of LC3-associated Phagocytosis. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

The Role of LC3-associated Phagocytosis in the Development of Diabetes Mellitus. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

The Role of LC3-associated Phagocytosis in Autoimmune and Inflammatory Disorders. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Clinical Evaluation of LLLT, Buprenorphine, Chlorhexidine in Clinical Disease. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Mechanistic Study of the Impact of Environmental Factors on Neurological Disorders. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

The Role of LC3-associated Phagocytosis in Arthritis and Colitis Models. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Redacted by agreement Reproductive Biology Investigations. **(Continue with changes – see amendment)**

Redacted by agreement

Redacted by agreement

In Vivo Study of the Role of Acetylcholine in Learning and Memory. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

The Role of Tlr5 in Inflammatory and Fibrotic Disease. **(Continue with no changes)**

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Genetic Analysis of MTAs. **(Continue with no changes)**

Maintenance of NIEHS-generated, Complex Genetically Modified Mouse Models. **(Continue with no changes)**

Physiological Function of Glis2. **(Continue with no changes)**

Metabolism and Disposition Studies of Ammonium 2,3,3,3-tetrafluoro-2-(heptafluoropropoxy)propanoate (GenX). **(Continue with changes – see amendment)**

Refinement in Microbial Flora Depletion. **(Continue with no changes)**

Evaluation of Corticosteroid Receptor Functions in Intestinal Enterocytes. **(Continue with no changes)**

Pregnancy-induced Epigenetic Changes in Female Mouse Mammary Ductal Epithelium. **(Continue with no changes)**

The Role of DNASE1L3 in Tumorigenesis. **(Continue with no changes)**

Characterization of PPIP5K KI mice. **(Continue with no changes)**

Effects of Perfluoroalkyl Substances on Mouse Puberty and Obesity Related Outcomes. **(Continue with no changes)**

Terminal Nucleotidyl-Transferases (TENTs) Animal Protocol. **(Continue with no changes)**

Transgenerational effects of in utero Arsenic Exposure on Reproductive Development and Metabolism in Mice. **(Continue with no changes)**

Assessment of Gestational Hypertension in Mice. **(Continue with no changes)**

Development in a Dish: An Ex-vivo Fetal Mammary Assay. **(Continue with no changes)**

## SUBMISSIONS PREVIOUSLY REVIEWED AND NOT APPROVED – REQUIRING MODIFICATIONS TO SECURE APPROVAL

Project Number, Branch	Principal Investigator	Project Title	NA Date Reviewer
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Redacted by agreement

**MINUTES OF MEETING**  
**NIEHS ANIMAL CARE AND USE COMMITTEE**  
**September 24, 2020; 1:00 pm**  
**Virtual Meeting through Zoom**

Members Present: Dr. Don Cook (Chair), [Redacted by agreement]  
[Redacted by agreement] Dr. Kathy Laber, [Redacted by agreement]  
[Redacted by agreement] (14/15 members present; quorum assured)

Also Present: [Redacted by agreement]  
[Redacted by agreement]

Absent: [Redacted by agreement]

The minutes of the August 27, 2020 ACUC meeting were approved.

ARAC Meeting: Dr. Cook summarized the September 23, 2020 ARAC meeting. Funding for the proposed Center for Disease Research building on the main campus is in the proposal stage but has been slowed due to a growing aversion to animal testing within Congress. In light of these delays, Dr. Cook reminded the committee that the mission of the ACUC is to ensure animal research is done appropriately and humanely. An NIH FOIA officer was asked to attend the ARAC meeting to discuss the significant increase in FOIA requests. The requests to NIH have increased by 49% over the past year and have included requests for video monitoring, mostly for NHP, but also for resident-intruder tests in mice. [Redacted by agreement] summarized the ARAC guideline; Preparing USDA Annual Reports that were reviewed and approved and described a proposed change to the Animal Welfare Act Regulations that will eliminate the USDA requirement for annual review of protocols. Protocols will be reviewed every 3 years, aligning the AWA with PHS Policy. [Redacted by agreement] also reminded the committee that the fall semiannual report is due to OACU by October 30, 2020 Dr. Laber presented the ARAC subcommittee's findings regarding the Euthanasia of Rodent Fetuses and Neonates guideline. There was consensus that some content of the guideline is contrary to the 2020 AVMA Euthanasia Guidelines and that the need for a separate guideline for this subgroup is no longer needed. The ARAC approved the removal of the guideline and it was agreed that if found necessary in the future that portions of the guideline could be incorporated into another active ARAC Guideline. The next ARAC meeting is scheduled for October 21, 2020.

Monthly VMS Report: VMS is actively monitoring one study with no adverse events to report.

COVID-19 update: [Redacted by agreement] reported to the committee that the daily ART calls for the NIH animal program has now been decreased to twice weekly.

NIEHS Guideline – Recommended Drug Doses, Routes, Needle Size, and Needle Use in Mice and Rats: [Redacted by agreement] summarized the new guideline that sets the maximum number of times a needle can be re-used. Ideally, needles should be changed between each injection. Needles should be changed after a maximum of 5 SQ injections and it is recommended that new needles be used for IV, IM, or IP injections.. The committee challenged the recommendation to change needles for IP terminal injections. The guideline will be updated to incorporate these exceptions and the revision will

circulated to the ACUC for comment. A final revision will be presented to the committee at the October ACUC meeting.

Fall Semi-Annual Report: [Redacted by agreement] presented the Fall 2020 semi-annual report. NIEHS utilizes the OLAW checklist for the fall review of the animal program. The facility, laboratory, and program summaries will be combined into the OACU semi-annual report template and will be presented to the ACUC at the October meeting. The report will be submitted to the Scientific Director and NIH OACU by October 30, 2020.

Distributed to ACUC

Email:

None

Distributed to NIEHS ASP Participants

Email:

Transnetyx Seminar on new tool for mouse colony management; September 9, 2020 (Laber)

Each of the following proposals and amendments was reviewed for all issues covered in the instructions to investigators including rationale for work, appropriateness of animal model and animal numbers used, method of euthanasia, surgical and post-operative care and issues related to pain and distress of animals. All actions, unless noted otherwise, reflect a unanimous action on the part of committee members present and no minority viewpoints were expressed during the ACUC deliberations.

#### NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - PROPOSED FOR FULL COMMITTEE REVIEW

Project Number, Branch	Principal Investigator	Project Title	ACUC Reviewer
[Redacted by agreement]	[Redacted by agreement]	<b>(Approved)</b> Use of Transgenic and Knockout Mice to Study Zfp36 (TTP), Zfp36l1 (TIS11B), Zfp36l2 (TIS11D), and Zfp36l3; <u>(Add More Animals:</u> Add 15 CD45.1 mice as bone marrow donors; <u>Change in Animal Procedures:</u> Add hypothermia anesthesia followed by temporal vein injections of bone marrow into neonates to rescue the phenotype and fostering post-injection).	[Redacted by agreement]

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agreement

Redacted by  
agreement

**(Approved)** Genetic Analysis of MTAs;  
(Change in Animal Procedures: Add  
administration of TNP-Ficoll and TNP-LPS;  
Add transfer of mice to the UNC behavior  
core for phenotyping; Add anogenital  
distance measuring using calipers, Faxitron  
and body mass analyzer procedures).

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agreement

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agreement

Toxicity Caused by NTP/NIEHS Relevant  
Chemicals or Environmental Stressors. **(No  
Longer Active)**

## NIEHS ANIMAL STUDY PROPOSALS AND AMENDMENTS - REVIEWED BY DESIGNATED MEMBER REVIEW

Project Number, Branch	Principal Investigator	Project Title	Approval Date Reviewer
Redacted by agreement	Redacted by agreement	Breeding Protocol for Studies of the Role of Cholesterol Trafficking in Lung Inflammation. <b>(Renewal)</b>	Sept. 14, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Redacted by agreement Breeding Protocol; ( <u>Add More Animals</u> : Add 288 Wnt7aCrexCtcf-flox and 288 Wnt7aCrexZmiz1-flox mice for breeding and colony maintenance).	Sept. 1, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Redacted by agreement Breeding Protocol; ( <u>Add More Animals</u> : Add the following new strains and a total of 2,016 mice for breeding and colony maintenance: Prl8a2iCre x Prflox, SUN1, Prl8a2iCre xSUN1, PgriCreERT2xSUN1, Wnt7a-CrexSUN1, Ddxx4creERT2xSUN1, and Myh11iCreERT2 xSUN1).	Sept. 9, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Mechanistic Study of the Impact of Environmental Factors on Neurological Disorders; ( <u>Change in Animal Procedures</u> : Add pilot study for use of sipper tube device, which uses an infrared beam break to record the number and duration of drinking events).	Sept. 1, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Mechanistic Study of the Impact of Environmental Factors on Neurological Disorders; ( <u>Add More Animals</u> : Add 160 of each of the following strains: Agrp-Cre, DAT-Cre, Mc4r-Cre, NPY-Flp, NPY-	Sept. 24, 2020 Redacted by agreement

Flp/DAT-cre, and NPY-Flp/Mc4r-cre;  
Change in Animal Procedures: Add 20% ethanol consumption to previously approved procedures including viral injection surgery and optical fiber or GRIN lens implant and high fat diet).

Redacted by agreement	Redacted by agreement	Redacted by agreement	Reproductive Biology Investigations; ( <u>Add More Animals</u> : Add 216 Ddx4CreERT2-mTmG, 216 Ddx4CreERT2Wnk1flox, 36 Myh11iCreERT2mTmG, and 3 PgriCreERT2mTmG mice; <u>Change in Animal Procedures</u> : Add perinatal Tamoxifen dosing to study developmental effects (in addition to 4-10 week old adults) and an endpoint extension of up to 1 year post-Tamoxifen treatment).	Sept. 1, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement	Redacted by agreement	Reproductive Biology Investigations; ( <u>Change in Animal Procedures</u> : Add hCG dose of 5 IU for mice older than 21 days (previously approved for 2.2 IU); Add vaginal smear procedure).	Sept. 11, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement		Metabolic and epigenetic regulation of cancer and stem cell differentiation; ( <u>Add More Animals</u> : Add 64 Balb/cJ, 64 NSG CD34FL, 128 C57BL/6J, 128 Tcra, and 128 CD8 KO mice; <u>Change in Animal Procedures</u> : Add previously approved cell lines MC-38, B16.F10, and 4T1 to approved methionine diet procedure).	Sept. 11, 2020 Redacted by agreement
Redacted by agreement	Redacted by agreement		Terminal Nucleotidyl-Transferases (TENTs) Animal Protocol; ( <u>Add More Animals</u> : Add 160 Cre-Ert2 Tut4 Del Tut7-flox ID4-GFP and 168 DBA ID4-GFP mice for breeding and colony maintenance).	Sept.18, 2020 Redacted by agreement

## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – REVIEWED BY VETERINARY VERIFICATION AND CONSULTATION

Project Number, Branch	Principal Investigator	Project Title	Approval Date/ Vet Reviewer
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Redacted by agreement	Redacted by agreement	Chemokine and Toll-like Receptor Adaptor Function in Pulmonary Inflammation; ( <u>Other Changes:</u> Add Kolliphor as a vehicle to increase solubility of some compounds).	Sept. 3, 2020 Redacted by agreement
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## AMENDMENTS TO NIEHS ANIMAL STUDY PROPOSALS – MINOR ADMINISTRATIVE CHANGES

Project Number, Branch	Principal Investigator	Project Title	Approval Date
Redacted by agreement	Redacted by agreement	Training and Development of Technical and Surgical Procedures, Analgesic and Anesthetic Protocols; ( <u>Add a New Participant:</u> Add Redacted by agreement)	Sept. 4, 2020
Redacted by agreement	Redacted by agreement	Development and Refinement of Analgesics in Laboratory Animals; ( <u>Add New Participants:</u> Redacted by agreement Redacted by agreement Redacted by agreement)	Sept. 4, 2020
Redacted by agreement	Redacted by agreement	Breeding and Maintenance Protocol for Studies of LC3-associated Phagocytosis as a Critical Regulator of Inflammation; ( <u>Add a New Participant:</u> Add Redacted by agreement Redacted by agreement)	August 31, 2020
Redacted by agreement	Redacted by agreement	Tissue and Sample Harvest for the Study of LC3-associated Phagocytosis; ( <u>Add a New Participant:</u> Add Redacted by agreement Redacted by agreement)	Sept. 2, 2020
Redacted by agreement	Redacted by agreement	The Role of LC3-associated Phagocytosis in the Development of Diabetes Mellitus; ( <u>Add a New Participant:</u> Add Redacted by agreement)	Sept. 2, 2020
Redacted by agreement	Redacted by agreement	The Role of LC3-associated Phagocytosis in Autoimmune and Inflammatory Disorders; ( <u>Add a New Participant:</u> Add Redacted by agreement)	Sept. 2, 2020
Redacted by agreement	Redacted by agreement	Clinical Evaluation of Low Level Laser Therapy (LLLT), Buprenorphine, Chlorhexidine in Clinical Disease	Sept. 4, 2020

Models; (Add a New Participant: Add

Redacted by agreement

Redacted by  
agreement

Redacted by  
agreement

The Role of LC3-associated  
Phagocytosis in Arthritis and Colitis  
Models; (Add a New Participant: Add

Sept. 2, 2020

Redacted by agreement

Redacted by  
agreement

Redacted by  
agreement

Refinement in Microbial Flora Depletion;  
(Add a New Participant: Add

Sept. 4, 2020

Redacted by agreement

Redacted by agreement

## ANNUAL REVIEW OF ANIMAL USE ACTIVITIES – Reviewed by Designated Member Review by

Redacted by agreement

**Project Number,  
Branch**

**Principal  
Investigator**

**Project Title**

Redacted by agreement

Redacted by  
agreement

Host Resistance to Viral and Bacterial Infections in Multiple  
Strains of Mice. **(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Mechanism of Fertilization. **(Continue with no changes)**

Redacted by agreement

Redacted by  
agreement

Effects of Estrogen in Differentiation. **(Continue with no  
changes)**

Redacted by agreement

Redacted by agreement

Production and Breeding of KO/TG Mice in the Knock Out  
Core. **(Continue with no changes)**

Redacted by agreement

Redacted by  
agreement

NIEHS Research Animal Health Surveillance Program.  
**(Continue with no changes)**

Redacted by agreement

Redacted by  
agreement

Validation of Viral Vectors for Gene Delivery In-Vivo.  
**(Continue with no changes)**

Redacted by agreement

Redacted by agreement

Regulation and Function of Mineralocorticoid Receptors in  
Hippocampal CA2 Neurons. **(Continue with no changes)**  
Metabolism and Disposition Studies of 2,4,6  
Tribromophenol(TBP). **(Continue with no changes)**

Redacted by agreement

Redacted by  
agreement

Redacted by agreement

Redacted by  
agreement

The Neural Regulation of Physical Activity. **(Continue with  
no changes)**

Redacted by agreement

Redacted by  
agreement

Development of Cholinergic Neurons in the Brain.  
**(Continue with no changes)**

## SUBMISSIONS PREVIOUSLY REVIEWED AND NOT APPROVED – REQUIRING MODIFICATIONS TO SECURE APPROVAL

Project Number, Branch	Principal Investigator	Project Title	NA Date Reviewer
Redacted by agreement			