

School of Medicine and Public Health Animal Care and Use Committee Open Session – January 6, 2020

Present (voting):
Present (nonvoting):
Guests:
Absent:
Dr. called the meeting to order at 8:30 a.m.
Approval of Open Session Minutes of December 2, 2019
moved to approve the minutes with minor editorial modifications. The vote was unanimous. Dr. provided an update from the minutes, confirming that a consultation took place regarding protocol M006273 as directed by the committee. Dr. confirmed that the PI of protocol M005630 is aware that he needs to begin splitting up this complex protocol as per the committee.
Annual Reapprovals (January)
moved to approve the annual updates. The vote was unanimous with abstaining. Dr. summarized feedback from the annual reapprovals, noting none of the protocols on the list use USDA-covered species.
Logs: Designated Review/other (January)
The committee reviewed the designated review and veterinary verification and consultation (VVC) logs. Dr. noted the large number of VVCs performed in December, and confirmed all changes were acknowledged as appropriate for VVC.

Protocol Reviews

Ms. provided a brief explanation of a change in the protocol form that requires individuals who request to transport research animals in privately-owned vehicles, or non-designated departmental or fleet vehicles, to attach a completed permission form to the protocol. She reminded committee members to verify the forms are attached when reviewing protocols.
M005303-R01-A02: Studies of the cochlear nuclei – Reviewers noted this amendment was called for full committee review from designated review due to concerns with food restriction of mice and the use of collars to reduce oral activity that could affect data recording. Discussion ensued. The PI will be asked to provide specific criteria for identifying animal weakness due to food restriction, to provide additional scientific justification for proposed methods of reducing aural activity and what alternatives were considered, clarify if laboratory staff will provide husbandry care, and to make other changes. Moved to require modifications to secure approval and to require the PI to have an in-person consultation with Dr. and a scientific member of the ACUC regarding the committee's concerns. The vote was unanimous.
M005690-R01: Characterization of anti-tumor immune responses in mice - Discussion of the protocol ensued. The PI will be asked to update the chemical hazards information, to clarify the post-operative analgesics for mini-pump surgeries, and to make other changes. Moose
M005719-R01: Genetic Mouse Models for Primary Congenital Glaucoma - Discussion of the protocol ensued. The PI will be asked to revise the description of animal numbers justification, to clarify the method of animal transportation, and to make other changes. moved to require modifications. The vote was unanimous.
M006277: pH Detection in Acute Compartment Syndrome in Swine - Discussion of the protocol ensued. The PI will be asked to clarify how pressure in the limb will be returned to normal post-procedure, to describe safety precautions that will be followed when on farm premises, and make other changes. moved to require modifications to secure approval. The vote was unanimous.
Committee members briefly discussed an amendment currently under consideration for designated review eligibility. A concern with the lack of detail in the plan to monitor infected mice for lung sepsis was raised. Dr. asked committee members to carefully consider if the amendment is eligible for designated review or would be more appropriately reviewed at a convened ACUC meeting, and to indicate their choice in the ARROW system.
Post-approval Monitoring: Report from Senior Program Veterinarian
Dr. had no report for open session.
Post-approval Monitoring: Report from Biomedical Research Model Services (BRMS)
Dr. had no report for open session.

Post-approval Monitoring: Report from Animal Program Assessment Specialists Mr. had no report for open session. **Committee Training** Ms. presented information about scientific merit review, the IACUC's role in conducting scientific merit review in the context of reviewing protocols, and provided examples of how some common protocol review questions in fact are questions about scientific merit (see attached). She highlighted the positions of NIH Office of Laboratory Animal Welfare (OLAW) and the Guide regarding scientific merit review by IACUCs, which state that IACUCs may ask questions about scientific merit review as part of considering if the proposed work with animals is ethical. Drs. and briefly described their experiences participating in grant reviews, and contrasted the questions raised during grant reviews with the questions raised by animal care and use committees. Discussion ensued. Dr. reminded members that if the committee is unsure of the scientific value of proposed work that they can require the PI to conduct a pilot study, or a limited number of procedures, and evaluate those outcomes before approving a larger-scale project. Members thanked Ms. for presenting this topic. Approval of Semiannual Program Review Minutes of November 25, 2019 Discussion ensued. moved to approve the minutes with minor editorial modifications. The vote was unanimous. Dr. said he will draft a letter to the Institutional Official and circulate for final comment, and members' signatures will be collected at the February meeting. **Other Business** reported that the All Campus Animal Planning and Advisory Committee (ACAPAC) is considering making links to readability scoring programs available to PIs. These programs may help PIs ensure that the language used in research protocols is understandable to laypersons. briefly summarized a recent inspection by the USDA Veterinary and Medical Officers (VMOs) that included the SMPH animal facilities and records. No noncompliant items were cited. called for other business for open session. Hearing none,

The meeting was adjourned from Closed Session without reconvening into Open Session.

moved to adjourn into Closed Session for discussion of research protocols or other documents containing confidential proprietary information and personnel matters relating to such research protocols, pursuant to Wisconsin Statutes Section 19.85(1)(c), (d), (e), (f), and (g). The vote was

unanimous by roll call.





School of Medicine and Public Health Animal Care and Use Committee Closed Session – January 6, 2020

Present (voting):	(for),	,
Present (nonvoting):			I
Guests:			
Absent:			
Approval of Closed S	Session Minutes of Decem	ber 2, 2019	
The vote was unanimous is working with steps that are taken to surgeries.	th the PI of the cardiovascu	n update from the mir	nutes, stating that Dr.
Inspection Reports			
list of rooms that have inspections and are no that the SMPH ACUC can be reactivated upo	of Spring inspections was centre not been used for live animal currently listed on approve decommission these room on PI and an acceptable AC mmission the list as present	mal work since the Sp yed protocols (see atta as for animal use, noting UC inspection. Discu	ring 2018 semiannual ched). She recommended ng that any of the rooms assion ensued.
Post-approval Monit	oring: Report from Senio	or Program Veterina	<u>rian</u>
Dr. had	d no report for closed session	on.	
Post-approval Monit	oring: Report from Biom	edical Research Mod	del Services (BRMS)

Dr. reported that servers supporting the environmental monitoring system for BRMS facilities, and other animal facilities on campus, and the sick animal reporting app have been updated and physically moved from the and the local physically moved from the local physical phy
Post-approval Monitoring: Report from Animal Program Assessment Specialists
Mr. provided additional information about the USDA Veterinary Medical Officers (VMOs) recent inspection, describing their site inspections of USDA-covered species housed at and and and and and and and and are and and and and are and are and and are and and are are and the ACUC's active oversight of the core.
Cores and Compliance – Report
Ms. presented a report of feedback from four research cores and how each core ensures that animal activities performed by the core staff, or by users of the cores, are described in an ACUC-approved protocol (see attached). She said that all four cores determine if the proposed work is covered by core protocols, and instruct the clients to amend their independent protocols to include the use of the core or to clarify what work will be performed by the PI versus the core staff. Ms. said the core staff provide standardized text to PIs for them to use to amend their protocols, however, none of the cores specifically request a copy of the PI's IACUC-approved amended protocol to verify any such changes have been made. She said that the SMPH ACUC may wish to consider requiring the cores to add a confirmation statement to project documentation that indicates both the client and the cores' staff understand that all animal activities must be described in an approved IACUC protocol before they are performed. Discussion ensued. The committee requested detailed information or examples of the exact documentation for each core to which such a statement would be appended. Dr. will follow up and report back to the committee.
Other Business
Ms. reported that a waiver from Lab Animal Surgery training was granted to , a DVM clinical instructor at the School of Veterinary Medicine.
Dr. called for other business for Closed Session or additional business for Open Session. Hearing none, Dr. adjourned the meeting from closed session at 10:35 a.m.

LOGS for SMPH ACUC – January 2020

Designated Review New/Renewal

PI	Prot #	Date Rec'd	Title	Species	N/R

Designated Review Amendment

PI	Prot #	Date Rec'd	Title	Species	Sum of change
	M5554- R01-A01	11/18	Molecular Imaging of Breast Cancer	Mouse	+IM injection, +estradiol valerate
	M5844- A01	11/18	Rational molecular targeting in high-risk cancer	Mouse	+addl substances, +addl imaging, +blood collection
	M5387- R01-A01	11/19	Role of IgM in transplant glomerylopathy	Rat	+addl animals
	M5625- R01-A01	11/20	Cytochromes P450: Expression and Regulation	Mouse	+addl housing
	M5279- R01-A07	11/20	Neural mechanisms of loss, recovery and alterations of consciousness	Mouse	+KW-6002 (adenosine antagonist), +increased injections
	M5405- R01-A01	11/21	Cell motility mechanisms using zebrafish	Zebrafish	+Candida fungus injections
	M5020- R01-A01	11/26	Zebrafish as a model for the blood-brain barrier	Zebrafish	+blood-brain permeability assay, +Dox treatment, +fluorescent dextrans
	M6020- A02	11/30	Molecular Elucidation of Physeal Growth Acceleration after Periosteal Resection	rabbit	+addl animals, + resection of femur
	M5217- R01-A04	11/29	Investigation of the virulence of toxoplasma gondii and its protection against other infections	Mouse	+diet
	M5303- R01-A02	12/4	Studies of the cochlear nuclei	Mouse	+overnight food fast, +restraint
	M6254- A01	12/6	Immunotherapy for Malignant Glioma	Mouse	+cell lines with humanized mice

M6075- A05	12/9	Neuro-and immunopharmacology in substance use disorders	Mouse	+oral corticosterone, +lipopolysaccharide admin
M5342- R01-A01	12/9	Mouse models of human cancer	Mouse	+diet study, +microsatellite instable colorectal cancer model, +lentivirus study
M6243- A01	12/12	Nanogenerator-Driven Self-Activated Electrical Stimulation for Enhanced Wound Healing	Mouse	+addl mice, +wound healing between mouse/human skin study
M5952- A06	12/12	Membrane excitability and secretion from nerve endings	Mouse, rat	Personnel update
M6171- A05	12/13	Molecular mechanisms of cerebral ischemia	Mouse, rat	+gu microbiota on MCAO model of stroke
M5786- A05	12/17	Virulence Factors in fungi	Mouse	+oxylipins study
M5597- R01-A01	12/17	Mechanisms of lung injury and fibrosis	Mouse	Change in food consumption

Veterinary Verification and Consultation (VVC) Remember to notify safety

PI	Prot #	Date Rec'd	Title	Species	Sum of change
	M5165- R01-V03	11/19	Cytoskeletal dynamics in Neuronal development	Mouse, rat	+genotyping/Id
	M6211- V01	11/20	The ionic properties of vertebrate hair cells	Mouse	+isoflurane anesthesia
	M5210- R01-V01	11/21	Regulation of pancreatic beta-cell mass	Mouse, rat	Chgd filtration of Avertin
	M6163- V02	11/20	Nerve Stimulation Strategies in Swine	Pig	Correct dose description, +glucose monitoring
	M5204- R01-V02	11/21	Potential interventions in a rodent model of antibody mediated rejection	Mouse, rat	+addl blood collection site
	M5279- R01-V04	11/21	Neural mechanisms of loss, recovery and alterations of consciousness	Mouse	+KW-6002 (adenosine antagonist), +increased injections

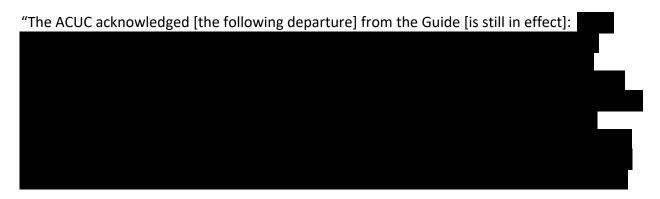
M5486- R01-V02	11/21	Lingual and laryngeal muscle plasticity	Rat	+3 days post op monitoring, clarify training paradigm
M5922- V01	11/22	Mitochondria in Progressive Multiple Sclerosis	Mouse, rat	+nicotinamide
M5544- R01-V03	11/26	Noninvasive tissue ablation using focused ultrasound histotripsy	Pig	+optional CT imaging
M5204- R01-V03	12/3	Potential interventions in a rodent model of antibody mediated rejection	Rat, mouse	+saphenous blood collection
M5512- R01-V02	12/5	Swine models of cardiovascular disease	Pig	More flexible analgesia admin
M5224- R01-V01	12/6	Studying Beta-Amyloid mGluR5 and Diet in Neurological disorders	Mouse	+new location
M2302	12/9	Antibodies to Clostridium botulinum toxin	Rabbit, mouse	+disposition (adoption)
M5544- R01-V04	12/10	Noninvasive Tissue Ablation Using Focused Ultrasound Histotripsy	Pig	Modification of pre-op meds to change atropine use
M6151- V04	12/10	Study of HSV-1 latency and Reactivation	Mouse, rabbit	Updated euthanasia
M5630- R01-V01	12/12	Development of Multimodality Molecular Imaging Agents and Electrical nanogenerator applications for animal studies	Mouse, rat	A procedure described in the rat section was not described in the mouse section during the renewal process. This corrects that oversight.
M5196- R01-V01	12/13	Characterization of a new microwave ablation device	Pig	KCl, paralytics, analgesia and anesthetic modified for flexibility, +NSAIDS
M53V69- R01-02	12/16	Non-invasive assessment of effectiveness of resuscitation after hypoxia induced cardia arrest in a pig model	Pig	+antihistamine added to help reduce potential histamine release, and resulting hypotension and tachycardia, with administration of oleic acid
M6163- V03	12/14	Nerve Stimulation Strategies in Swine	Pig	Refinements for prolonged anesthesia, +bicarb & destrose as clinical support

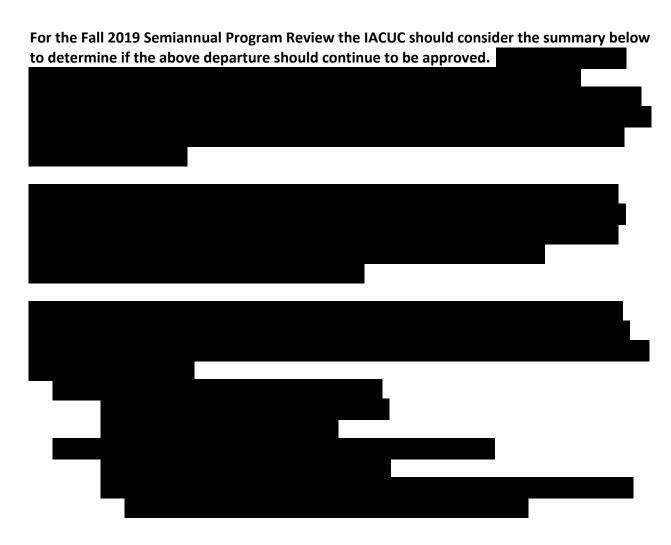
	M5889- V01	12/17	In vivo evaluation of novel tumor- targeted therapies and adoptive immunotherapies for cancer	Mouse	+new contrast agent (5-ALA)
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Dual School Review

PI	Prot #	Date Rec'd	Title	Species	Addl ACUC
	V5847-A05	11/21	In Utero programming of Adult Diseases	Rat	
	V5173-R01-A09	11/21	Effects of Hormones, Toxins, Oxygen and Growth Factors on Brain Glia and Neurons	Mouse, rat	
	G005698-R01	11/26/19	Nonhuman Primate Bone Marrow Transplantation Model	Cynomolgus macaque	
	G005154-R01- A02	11/27/19	Control of GnRH neurons and puberty	Rhesus, Macaque	
	G006085-A02	11/30/19	Brain Gut Axis and Vagus Nerve Stimulation	Rhesus Macaque	
	V5703-R01	12/6	Periosteal transection to accelerate bone growth by afocused ultrasound	Sheep, rabbit	
	A005694-R01	12/11/19	Swine Models of Chronic and Inducible Tumors	pig	

The SMPH IACUC Spring 2019 Semiannual Program Review report to the Institutional Official contained the following:





UW-Madison Animal Care and Use Semi-Annual Program Review Fall 2019 SMPH

IACUC III. Personnel Qualifications and Training

RARC Training courses (May 1, 2019 - October 31, 2019)

- 2231 courses accessed and completed campus wide, 331 from SMPH
 - o 1497 not attached to protocols
 - o 734 attached to protocols
 - 331 from SMPH
- 1422 distinct individuals, 236 distinct individuals from SMPH
 - Some individuals take multiple courses

Hands-on

- 694 hands-on training completed campus wide, 317 from SMPH
 - o 76 SMPH completed Lab Animal Surgery/LAS Aquatics
 - o 241 SMPH Species Specific completed
 - Online module/hands on training
 - Mouse(140), Rat (53), Swine (23), Zebrafish (9), Cat (5), Rabbit (5),
 Xenopus (4), Fish (2),
- Additional hands-on training requests: 119 sessions (512 students) campus wide, 67 SMPH sessions (90 SMPH students)
 - o Returning students for additional help/refresher
 - Injections: cardiac, intranasal, intraperitoneal (IP), intratibial, jugular, oral gavage, retro-orbital (RO), tail vein
 - Bleeding techniques: maxillary, retro-orbital, tail, cardiac
 - Surgical: carotid artery isolation, gonadectomy, nephrectomy, micro-infusion,
 - Pathology
 - Perfusion
 - Stereotax
 - Mouse refreshers: ear notch, ear tags, tail snip, tattoo, euthanasia, cervical dislocation
 - Rabbit refresher

Waivers

- Approval granted from Dr. /IACUC
- 33 waivers granted campus wide, 6 from SMPH
 - Waived for: Lab Animal Surgery (4), Cat (2)

Revocations

- We have not had to report any revocations to the IACUC

Meet and Greets

- 9 SMPH PIs out of 16 PIs campus wide

Outreach

- o Dairy Cattle Outreach Event, Spring Finals Week, 339 participants
- o Campus Visitor's Program
 - Belleville Elementary, Waunakee High School, PEOPLE, Rosendale Middle School
- o Research Professionals Conference

Other Training Updates

0

- Refresher Training/Train the Trainer/Continuing Education
 - o Dog, Cat, Horse, Swine, isoflurane drop box, tail vein injections
- Online Modules:
 - o Animal User Recertification, Microisolator, Primate, Rat: Horse, LAS Pre-requisite on 02/03/2021

For Worksheet Section IV-A-B



Environment, Health and Safety

DIVISION OF FACILITIES PLANNING & MANAGEMENT

UNIVERSITY OF WISCONSIN-MADISON

Environmental and Occupational Health Summary Occupational Health Program Status October 2019

Compliance with Animal Contact Risk Questionnaire (ACRQ)

On October 11, 2019 the compliance rate* for ACRQ was 96% with 4123 enrolled. During the time period since the last report, those compliant with ACRQ review ranged from 91 to 95% with an average of 93%.

The Occupational Medicine staff reviewed 2245 ACRQ questionnaires in this time period.

Occupational Health Program for Service Personnel

Compliance for UW Madison staff enrolled in SPLAAAF was 90% on October 11, 2019. Compliance during the period since the last report has dropped slightly while EOH and FPM have been working to determine the complete list of staff required to be enrolled.

UW Health confirmed they are asking about animal allergies in pre-employment health assessment and if animal allergies worsen during work directing employees to contact their Employee Health Service.

Recent and Future Impacts

UHS has continued to meet with the electronic medical record vendor on a regular basis and EOH is engaged in these discussions and work groups including a cybersecurity risk assessment with UW Madison and beta testing of a web application version of the electronic medical record.

Effective July 1 2019 UHS EOH and Occupational Medicine were officially merged with FPM--Environment, Health and Safety department. Physically, all staff continue to be located at UHS. A MOU between FPM and UHS is being developed to address the Occupational Medicine functions that will continue to be located at UHS for the foreseeable future.

^{*} An individual is considered compliant when a UHS medical professional has reviewed the person's ACRQ and issued medical clearance to work with animals. Compliance rate is calculated as the number of enrollees with an approved ACRQ due date effective the month prior to date generated divided by the number of enrollees as provided to EOH (Animal Course Orientation Completion, RARC notice on animal protocol or specific class enrollment). For example, the above compliance rate was calculated by, identifying 165 enrollees who had never submitted an ACRQ, had submitted an ACRQ and not responded to questions from the provider, were due to have submitted annual ACRQ in September 2019 or earlier, had submitted recently and not yet reviewed. Thus, 4123-165/4123 * 100 is 96%

Committee Training May, 2019-October, 2019

Committee Training at Monthly Meetings

June: Post-Approval Monitoring (APAS)

August: Policy Review (Adverse Event Reporting)

September: Showtime! Should an IACUC oversee companion animal exhibition activities on campus?

(Lab Animal 48, 69-70)

October: On hold: What to report after a study is halted? (Lab Animal 48, 221-223)

Web Seminars

OLAW: The 4th R- Rehoming, Retirement and Release- June 13, 2019

NABR: Q&A with the USDA: Seventh Edition-July 11, 2019

OLAW: Application of the AVMA Guidelines for the Depopulation of Animals to Biomedical Research-

September 26, 2019

NABR: Cautionary Tails: FOIA and Other Threats to Sustainability of Animal Research- October 29, 2019

OLAW: 21st Century Cures Act: Next Steps

Archived NABR Web Seminars can be accessed at: http://www.nabr.org/nabr-members-only/webinars/ You will need to create a login, and be verified as being affiliated with a member organization (UW Madison) before you can access the member's only content.

Archived OLAW Web Seminars can be accessed at:

https://grants.nih.gov/grants/olaw/educational resources.htm#online-seminars

SMPH ACUC Program Review Fall 2019: Inspections

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Number of Inspections
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Regularly Scheduled Semi-annuals = 20

Make-ups for Semi-annuals = 7

New Procedure and/or Housing rooms = 7

Time Spent by voting members on regularly scheduled inspections

~49 hours, roughly the same as ~48 hours last Spring, down from ~65 hours Fall 2018.

Number of rooms on inspection list

Total = 701

Facility = 517

Lab = 150

Core Unit = 34

Minor Deficiencies = 56

Animal Welfare = 2, both anesthesia machined overdue for calibration

Expired Items = 38

Anesthesia, Analgesia or Euthanasia Drugs = 7

Other Drugs = 3

Other Medical Materials = 19

[1 Facility Repeat in , 1 Facility Repeat in , 2 Repeats in , 1 Second Facility Repeat in]

Cleansers/Disinfectants = 7

Food/Treats/Supplements = 1

Miscellaneous Items = 1 (Human First Aid Kit item)

Labels, Signage & Recordkeeping = 7 [1 Facility Repeat in

Housekeeping = 4 [1 Facility Repeat in

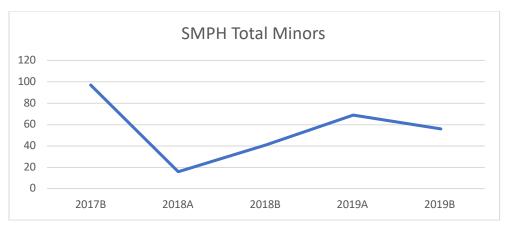
Safety = 2

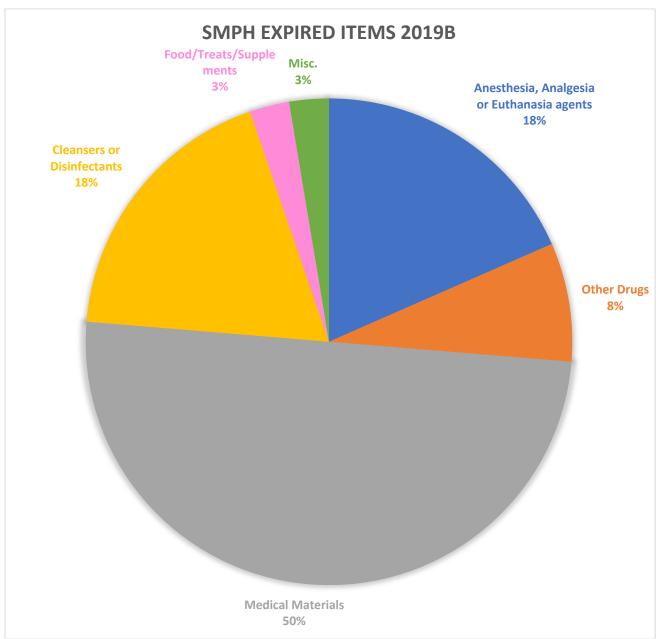
Infrastructure = 2

Significant Deficiencies = 0

Overdue Items = 0

for Worksheet Section VI-E cont.





SMPH ACUC Fall 2019 Protocol Review Statistics

Number of Protocols Reviewed and Approved in the six-month period preceding program review (4/15/2018 - 10/14/2019)

	Spring 2017	Fall 2017	Spring 2018	Fall 2018	Spring 2019	Fall 2019
New/Renewals	56	52	41	61	49	70
Amendments	117	116	113	142	133	145
Total	173	168	154	203	182	215

Turn-around time (in Days) for Protocols Reviewed and Approved during this period*

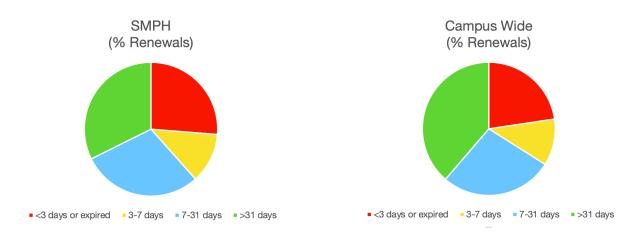
New or Renewals	Spring 2017	Fall 2017	Spring 2018	Fall 2018	Spring 2019	Fall 2019
Average	44	36	41	38	34	36
Median	41	35	36	37	31	36
Range	16-82	7-78	20-84	10-96	2-79	14-61

*Includes review time after submission (not including vet pre-review). Average vet pre-review time this cycle was 7 calendar days (same as last cycle).

Amendments or VVC**	Spring 2017	Fall 2017	Spring 2018	Fall 2018	Spring 2019	Fall 2019
Average	19	15	16	14	14	14
Median	16	13	15	13	14	14
Range	0-90	0-55	0-70	0-68	0-58	0-54

Includes changes approved through Veterinary Verification and Consultation (VVC) in which the changes may be implemented immediately after vet consultation. Twenty-nine percent of the SMPH protocol changes approved this cycle were via VVC. Although VVCs are in effect immediately upon consultation, the time required to process VVCs (update the protocol) averaged 3 calendar days. In July, 2019 the IACUC office began following up on VVCs that are not finalized within one week.

Average time between renewal approval and expiration



for Worksheet Section VI-H

As of October 31, 2019, the SMPH ACUC animal program currently have the following departures from the Guide approved in protocols (337 approved protocols total):

- 67 protocols approved for housing animals individually for experimental or veterinary reasons:
 - to prevent removal of imiquimod ointment used to create inflammation by conspecifics
 - o to accurately monitor food consumption by weighing food remaining in the cage
 - o to prevent conspecifics from damaging catheters / other implanted devices
 - o conditions described in the ASHER document (Policy 2011-042-v)
 - o other scientific justifications approved by the ACUC in protocols
- 8 protocols that involve restraint for more than one hour for the following reasons:
 - o to ensure study animals' ears receive a standard and controlled amount of exposure to vibration for biomechanics studies
 - o to hold awake mice under an imaging apparatus for an extended period of time
 - o to prevent retreat of study animals into sound shadows
 - o other scientific justifications approved by the ACUC in protocols
- 49 protocols that involve food or fluid regulation for the following reasons:
 - o to test whether every other day feeding affects adipose tissue accumulation and heat transfer properties of skin
 - o to motivate rodents to perform behavioral testing tasks
 - o prior to procedures such as blood draws and measurement of blood parameters, including leptin, insulin or glucose testing
 - o to minimize the effect of recent eating on the bio-distribution of the imaging agents administered and to prevent potential artifacts in the acquired images
 - o other scientific justifications approved by the ACUC in protocols
- 247 protocols that use non-pharmaceutical grade compounds for the following reasons:
 - o no pharmaceutical-grade formulation is available
 - o an equivalent veterinary or human drug is available for experimental use but the chemical-grade reagent is required to replicate methods from previous studies because results are directly compared to those of replicated studies
 - o the equivalent veterinary or human drug is not available in the concentration or formulation appropriate to meet experimental requirements
 - the available human or veterinary drug does not meet the nontoxic vehicle requirements for the specified route of injection or for the proposed research species

Spring 2019 program review data for comparison:

339 protocols total at time of report

- 71 protocols approved for housing animals individually for experimental or veterinary reasons
- 10 protocols that involve restraint for more than one hour
- 48 protocols that involve food or fluid regulation
- 246 protocols use non-pharmaceutical grade compounds

SMPH ACUC Program Review, Fall 2019: PAM and other reviews. Section VI, Part Q

Routine

We reviewed one rodent BSL3 study and found no concerns.

Directed

We continue visits to check-in on one zebrafish lab. The lab is doing an okay job generally but still needs reminders of various housekeeping items.

We completed one review that involved a Department of Medicine core. We identified concerns over protocol compliance, and completeness and accuracy of animal records. Ultimately, the PI elected to terminate this protocol, but completed retraining and took steps to improve both animal records and protocol compliance for other protocols involving the core.

We continue records reviews for three other protocols involving the Department of Medicine core noted above. Animal records have greatly improved since PAM review of the core began and we have not identified major compliance concerns with any of these three protocols.

Several other protocols were slated for review but because work had not occurred in the previous year or would not occur in the near future the reviews were not performed.

Congruence

There were 26 grant-protocol congruence checks done for SMPH [54 total].

Miscellaneous

We answered 28 controlled substance questions for SMPH PIs [50 total].

date	start	end	title	notes	travel (Min)	vm_ needed	attending
Thursday, January 16, 2020	8:30 AM	11:00 AM	SMPH- _Facility&Labs 2020A	Meet at loading dock.	15	2	
Wednesday, January 22, 2020	8:30 AM	10:40 AM	SMPH- Facility 2020A	No prior animal contact that day.	0	0	V: V:
Tuesday, January 28, 2020	1:00 PM	3:00 PM	SMPH- Labs-Fl 0-2 2020A		0	1	V:
Thursday, January 30, 2020	1:00 PM	3:00 PM	SMPH- Labs- 2020A		0	2	
Tuesday, February 4, 2020	8:30 AM	11:00 AM	SMPH-Facility 2020A		0	1	A: V:
Tuesday, February 4, 2020	1:00 PM	3:00 PM	SMPH-Labs-All 2020A		0	1	A: V:
Wednesday, February 5, 2020	1:00 PM	3:00 PM	SMPH		0	1	V:
Wednesday, February 12, 2020	1:00 PM	3:30 PM	SMPH- Facility&Labs 2020A		0	0	V: V:
Tuesday, February 18, 2020	8:30 AM	11:00 AM	SMPH- Facility&Labs & 2020A	Level 1 facility: No prior rodent contact that morning. Best to have vet for lab access.	0	1	A: V:

date	start	end	title	notes	travel (Min)	vm_ needed	attending
Wednesday, February 19, 2020	1:00 PM	2:00 PM	SMPH- 2020A		30	2	
Wednesday, February 26, 2020	8:30 AM	11:00 AM	SMPH- - Facility&Labs 2020A	Level 1 Facility No prior rodent contact that morning.	0	1	A: V:
Wednesday, March 4, 2020	1:00 PM	3:30 PM	SMPH-Facility 2020A		0	1	V:
Wednesday, March 25, 2020	8:30 AM	11:00 AM	SMPH- Facility&Labs 2020A	At least 1 Voting Member should be N95 fit-tested.	0	1	V:
Tuesday, March 31, 2020	1:00 PM	2:30 PM	SMPH-Labs_Labs_Labs_Labs_Labs_Labs_Labs_Labs_		0	1	V:
Wednesday, April 1, 2020	1:00 PM	3:00 PM	SMPHLabs- 2020A		0	1	V:
Thursday, April 2, 2020	1:00 PM	3:00 PM	SMPHLabs- 2020A		0	2	
Tuesday, April 7, 2020	1:00 PM	2:30 PM	SMPH		0	1	V:
Wednesday, April 8, 2020	8:30 AM	11:00 AM	SMPH-FacilityALL 2020A		0	2	
Tuesday, April 21, 2020	8:30 AM	11:00 AM	SMPH-CoreUnits 2020A		0	2	
Wednesday, April 29, 2020	7:00 AM	8:00 AM	SMPH Imaging Labs 2020A		0	2	

In this context to "decommission" an animal use room means to declare a previously approved room as unavailable, unneeded, or unsuitable for any further animal work. A room may be re-commissioned by treating it as a new room, including the requisite ACUC inspection.

Locations requested:

Building	Room	Last Inspected & Notes
		03/07/17
		08/03/17
		01/26/17
		02/20/19 (not active since 02/13/18)
		08/02/18 (not in active use since 07/27/17)
		07/27/17
		08/12/15 (not active since 08/19/14)
		01/31/17
		01/29/19
n		08/02/18
		08/30/17
		08/30/17
		09/21/16 (only tissue work since 03/22/16)
		09/21/16
		04/09/19
		03/14/17
		03/27/18
		03/27/18
		Only new room inspection, removed from protocol before next semi-annual.
		09/20/16
		08/31/17
		03/24/16
		08/31/17
		03/16/17
		10/03/17
		10/03/17
		Only new room inspection, removed from protocol before next semi-annual.
		07/30/15

Explanation: None of these rooms are currently listed on a protocol and have not been inspected for at least 3 inspection cycles. (Last inspection Spring 2018 or longer.)

annal Update

January 2020

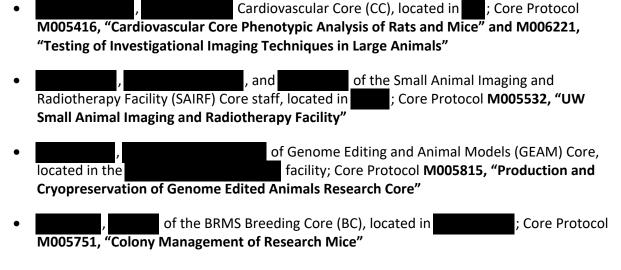
CHECK-OFF LIST

SMPH Re-Approvals January 2020

M02324-0-12-17

State filter no filter	Q PDF	Production of Botulinum Toxin in Foo	ď				ned by Ri ARLO
M02324-0- 12/13/17 1/17/18 1/17/20 1/16/21	Received Approved Next update	Research Biomedical Training Multiple surgeries 2/15/18 Approve by AU1 AU2 D USDA category		First Middle	Email @wisc.edu @wisc.edu @wisc.edu @wisc.edu @wisc.edu @wisc.edu @wisc.edu	S Role ^ Netid ? Pi staff staff staff staff staff staff staff	Bacteria: Clostridium botulinum Toxic: Clostridium botulinum Oo Alope Control
	_1 chideu	More programs Clear Save	Address, De		a, Phone, Procedures, Species Agents	Comments Euthanasia	- Kese
Received	~ Approved	Amendment	mus Euthanasia	28300 28300 PHS guidelines 20 Room Facility_House Facility_House		artments ^ Microbiology & Toxicology	Upiloaded to Amim
Grant title			Agency	Number	Congruence Comm	pents	
NOTE OF THE PROPERTY OF THE PR	and the second s						

Four Core directors were interviewed between November 20th and 27th to gather information about how the Cores ensure live animal activities conducted by or in the Cores are IACUC-approved. Persons interviewed were:



All four Cores conduct in-person meetings with clients who wish to use the services offered by the Cores. At these meetings, it is determined what work is requested and if that work is to be covered by each Core protocol or under the client's individual research protocol. All four Cores prepare some type of written document defining the project for the client. This may be a submission form (GEAM), a scope of work document (CC), a budget, or some similar document.

For GEAM, BC, and SAIRF, if work is requested by the clients that is not described in the Core protocol, then the Core directors tell the clients that such work must be described in the client's own independent IACUC-approved protocol. The Core directors counsel clients on how to prepare the amendment, and provide standardized text to the clients to include in these amendments. Clients are advised to include specific language indicating at what point animals will be tranferred from the research protocol to the Core protocol. The exception is the Cardiovascular Core. According to Dr. for UW PIs who do not hold a protocol (typically PIs outside of traditional biomedical research departments) he may amend the Core protocol M005416 to include research activities (full scale studies or one-time pilot work). Recently the SMPH IACUC has not approved these Core protocol amendment on the basis that independent research activities are not appropriate for a Core services protocol.

In circumstances in which clients transfer animals from their independent research protocols to the Core protocols (and back to the client's protocol, if needed), normal RARC animal transfer paperwork is submitted and approved by the RARC veterinary staff.

None of the four Cores specifically request a copy of the client's IACUC-approved amendment before initiating work on the client's behalf or before allowing "self-serve" clients (SAIRF and CC) to access Core areas and equipment. The lack of such verification presents the potential for noncompliance.

The SMPH IACUC may wish to consider requiring the Core to add a confirmation statement to the project paperwork that indicates the client and the Core staff understand that all animal activities must be described in an approved IACUC protocol before being performed.

CAN THE IACUC ASK QUESTIONS ABOUT SCIENTIFIC MERIT OR EXPERIMENTAL DESIGN DURING THE REVIEW OF A PROTOCOL?

<u>Yes.</u> Each IACUC member brings a unique perspective to the protocol review process – their own research experience, their educational background and training, their experience with specific species, and their personal beliefs. These inform a reviewer who is evaluating an animal care and use protocol to ensure the use of the animal model is scientifically and ethically justified.

Scientific merit defined: Webster defines merit as the "state of having worth, value or excellence." When the noun "merit" is combined with the adjective "scientific" it means of "scientific worth, value or scientific excellence." (Prentice, E.D., Crouse, D.A., Mann, M.D.; ILAR News 34(1-2): 15-16, 1992)

Scientific merit defined: In order for research to have scientific merit, "the research should be based on a significant hypothesis and, if possible, oriented towards uncovering an important biological mechanism. The hypothesis should be testable…by the proposed experiment." (Gordon, S.J.; Ortho. Res. 7:138-141, 1989)

Criteria for scientific merit:

- The hypothesis is testable (i.e. can be proved or disproved) by the experiment.
- The experimental design is appropriate and sound.
- The procedures selected will yield scientifically valid results.
- The results will be of sufficient [potential] value to advancement of science/knowledge.

Some members of the research community believe that IACUC review of proposed research should be limited to issues of animal health and wellbeing and should not extend to a consideration of scientific merit. They believe that because a significant proportion of funding requests undergo peer review by recognized experts charged with making decisions about the proposed science, including scientific merit, an IACUC with less specific expertise should not duplicate peer review efforts.

Definitions:

- Peer review: Choosing the best from a group of proposals all of which have scientific merit.
- IACUC review: Ensuring that the use of animal models is scientifically justified.

In the absence of peer review an institution - through its IACUC - has an obligation to ensure that an equivalent examination of methodology is undertaken. The IACUC, as society's gatekeeper, must determine that the proposed use of animals for scientific research ethical. In order for research to be ethical:

- It must have sufficient potential scientific or societal value which justifies the use of the animals.
- The ethical costs (harms) must be at least balanced by, and preferably outweighed by, the potential benefit(s).

Adapted from PRIM&R web seminar "Ethics, Scientific Merit Review, and Harm/Benefit Analysis in Animal Research", January 30, 2013

Regulations and Standards on Scientific Merit

- OLAW Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy), sections IV.C.I a, b, d, f.
- OLAW Frequently Asked Question #6, "Is the IACUC responsible for judging the scientific merit of proposals?" (http://grants.nih.gov/grants/olaw/faqs.htm#628):
- USDA Animal Welfare Act and Regulations, 9 CFR 2.31(d)(iii); 2.31(d)(iv)(A); 2.31(d)(x);
 2.31(e)(1)(2); 2.31 (e)(4); 2.32(a)
- The Guide for the Care and Use of Laboratory Animals (8th ed.), page 26 (The Role of the IACUC and Protocol Review)

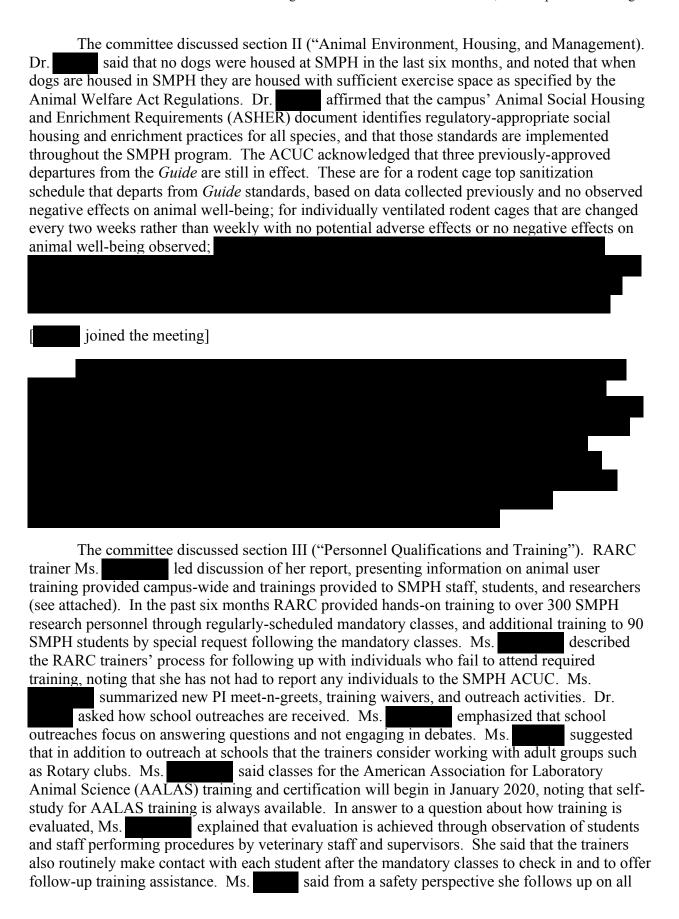
Advice on Writing IACUC Protocol Review Questions about Scientific Merit...

School of Medicine and Public Health Animal Care and Use Committee Program Review Open Session – November 25, 2019

Present (voting):	
Present (nonvoting):	
Guests:	
Absent:	
meeting is to perform t and Public Health. He regulations and PHS Po the UW-Madison Anin areas of strengths and o	explained that the purpose of today's he semiannual review of the animal program in the School of Medicine said that the program review is one of three activities that both the USDA olicy require of an IACUC. The committee will discuss each section of hal Care and Use Program Review Worksheet (see attached) and identify leficiencies. Dr noted the committee's comments from the eview have been provided in today's Worksheet for reference. He to the meeting.

Fall 2019 Semiannual Program Review

The committee discussed section I ("Physical Plant"). , finding in general the facilities are adequate for animal housing, procedures, and surgery, and have the necessary supporting equipment such as cage washers and autoclaves. The committee briefly discussed a previouslyacknowledged departure from a recommendation in the *Guide* regarding food storage conditions. Specifically, temperatures in some SMPH facility food storage rooms can occasionally exceed recommendations in the Guide. However, turnover rate of stored food is rapid and no animal health concerns have been noted that could be attributed to the food storage temperature. Dr. assured the ACUC that husbandry and veterinary staff will continue to monitor for any issues. The committee agreed to continue the approval of this departure. Another previouslyapproved departure regarding humidity levels in facilities that depart from Guide standards, primarily during the winter months, exists. Dr. stated that monitoring of humidity-related clinical issues by the veterinary staff will continue, with cases or trends reported to the ACUC as needed. He said no such clinical cases were seen in the past six months. Principal Investigators have been notified of the potential effect of humidity changes on research projects for the fall and winter of 2019.



biological exposures, such as needle sticks, and if she determines refresher training is required she contacts the RARC trainers. Overall the committee is confident in the training program for animal users in the SMPH animal program.

The committee discussed section IV ("Occupational Health and Safety," OHS), reviewing the report (see attached) provided by University Health Services (UHS), noting the high enrollment of researchers, students, service personnel, and security staff in the occupational health program. Ms. reported that sending safety training notifications through the ARROW system is working well and helping to improve compliance. She said the isoflurane workgroup continues to meet and assess high risk exposure areas to mitigate exposure, noting that Dr. is part of the workgroup. One high risk exposure area was identified in SMPH, and the lab is working closely with safety staff to reduce exposures. Ms. informational poster demonstrating proper anesthesia machine set-up is available by request from the RARC trainers, and the Environmental Health and Safety Department (EH&S) staff have updated guidance on safe use of isoflurane on their website. Ms. described the current status of the merger between the University Health Services (UHS) Occupational Medicine program and EH&S, and on the search for a new Assistant Vice Chancellor of EH&S. Finalists for the position have undergone interviews and a decision is expected soon. Dr. asked if UW Health employees undergo an annual risk assessment, similar to the annual update required of UW-Madison enrollees. Ms. will follow up on this question and report back.

The committee discussed section V ("Veterinary Medical Care"). Dr. noted that the policy for acclimating animals post-transport before undergoing survival procedures was recently updated to require 72 hours of acclimation. He said a shorter acclimation period may be requested from the veterinarians. In regards to veterinary anesthesia expertise and support, Ms. said that in the summer of 2019 the I.O. met with representatives of the School of Veterinary Medicine (SVM), and a proposal to fund 25% of a clinical faculty and boarded anesthesiologist at SVM exclusively for the campus-wide research animal program is currently under consideration by SVM and the Office of the Vice Chancellor for Research and Graduate Education (OVCRGE). Ms. said that updates on this proposal will be provided to the ACUC as they occur, and expertise in anesthesiology will continue to be available from SVM specialists. The committee members thanked the veterinarians for their valorous work with animal care and with veterinary pre-review of protocols. The ACUC also commended the BRMS ARTs on their attention to all aspects of animal welfare during daily care, transport, and the accuracy of the animal deliveries. Feedback from researchers regarding veterinary care demonstrates that the veterinarians are viewed very positively for their collaborative approach to veterinary care and research support. In general, the committee finds the program of veterinary care to be bosker.

The committee discussed section VI ("Institutional Animal Care and Use Committee").

Dr. thanked all of the members for their service and active participation, and expressed appreciation for the administrative support from RARC. He said that he and Dr. the newly appointed will be appreciation, will continue to work on identifying faculty to serve on the committee. Ms. provided information on the most recent inspections period (see attached), highlighting those deficiencies that were repeat incidents and noting that no deficiencies were classified as significant.

Dr. provided a report on committee training topics covered during the last six months, and on protocol review turnaround (see attached). She presented the number of protocols and amendments reviewed and approved over the last six months, noting 29% of changes to protocols were made via VVC. She summarized IACUC office discussions of possible strategies to avoid last-minute expiring renewals, noting these submissions place undue burden on the veterinarians and ACUC members to achieve timely review and approval. Dr. asked that for future reports that topics covered as committee training ad hoc during protocol review discussions also be included in the summary for semiannual program reviews. A summary of departures from the <i>Guide</i> in protocols approved by the SMPH ACUC was reviewed by Ms. noting no significant changes in the number of departures approved from the previous cycle (see attached). Dr. noted that toe clipping of rodents older than seven days of age is also a departure. Ms. gave a brief report on post-approval monitoring (PAM) activities conducted by the RARC Animal Program Assessment Specialists, including both routine and directed PAM reviews of protocols, grant-to-protocol congruency reviews, and support provided to SVM PIs answering questions regarding controlled substances (see attached).
The committee discussed section VII ("Institutional Official," I.O. The ACUC acknowledged that Dr. attended the September SMPH ACUC meeting. The ACUC agreed that it is beneficial to have the I.O. attend at least one ACUC meeting each year. Dr. said Dr. continues to participate in meetings of the All Campus Animal Planning and Advisory Committee. Committee members noted that they are confident that Dr. is familiar with the needs of research animal programs given her past experience as the SMPH ACUC chair.
The committee discussed section VIII (Program Integration) and section IX (Support of the Institutional Mission). The ACUC members agreed that communication between the ACUC, BRMS leadership and management, RARC management, and the Associate Dean of Research's office remain strong. The ACUC appreciates having been involved , and looks forward to continued involvement in high-level discussions of issues and initiatives that affect the animal program within SMPH. Regarding support of the institutional mission, the ACUC appreciates the funds that have been made available to support a veterinary anesthesiologist for the animal program and for pathology positions within RARC. Ms. briefly described a new service she is piloting to assist newly-hired faculty in entering the IACUC-approved protocols into the ARROW system, noting that she has assisted three new SMPH faculty to date.
Dr. called for additional comments. Hearing none, Dr. said that he will draft a report to the I.O. based on today's discussion and circulate it for edits, after which the members' signatures will be collected. moved to adjourn the meeting. The vote was unanimous. The meeting was adjourned at 12:50 p.m.
IACUC Administrator