ANIMAL CARE COMMITTEE MEETING MINUTES
JUNE 18, 2019

Attendees: Member 2, Member 6 Member 8, Member 9, Member 10, Member 11, and Member 30

Absent: Member 24

Guest: Member 39

1. Minutes

Minutes were sent for designated review determination.

2. Announcements

Member 2 indicated that follow-up on facility inspection was added under old business.

3. Old Business

a. Modification of Protocol 17-061 (10)

The Committee reviewed the PI's request to conduct a 24 IV infusion study in one animal for [redacted] using TFA salt formulation in endotoxin free micelle preparation. The Committee discussed that the PI was requesting to administer two bolus doses, 0.417 and 4.17 mg/kg, to be administered one hour apart followed by 24 hour infusion at `0 mg/kg/24 hours. The Committee discussed the following: that the animal requested was not naïve and this should be removed in D5b, that data regarding testing of [redacted]-11 in rats must be added to the table to show that this exact lot and formulation had been tested in rats, Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstention, and 0 recusals.

b. Update on Facility Inspections

Member 9 informed the Committee that all responses due by June 15th had been received and the action items addressed.

4. [redacted] Director's Legislative and Facility Update

The Committee discussed the following: 1) that a bid proposal for a new bulk dry heat sterilizer had been submitted and the intent was to have the unit installed before the end of the year which would significantly increase throughput capacity of rodent caging and provide a backup to current steam autoclaves which are in need of some significant control system upgrades and 2) that on June 28th Capital Programs would be interviewing

engineering and architectural firms for the [redacted] electrical and HVAC infrastructure upgrades.

5. [redacted] Update

a. Modification

Member 2 updated the Committee to the following activity during the past month: there was 0 modification approved via administrative level, 14 modifications approved administratively following veterinary consult, and 13 modifications approved via designated review this month. In addition, there were 35 protocols that added personnel, 0 with personnel deletions, 3 with addition of funding, and 0 addition to the holding protocol.

b. Continuations and Terminations

Member 2 directed the Committee's attention to the protocols for continuation and those terminated due to expiration or PI's request. The Committee discussed that all protocols had completed the appropriate continuation documents and a motion for designated member review for renewal the protocols was passed by the following vote: 7 in favor, 0 opposed, 0 abstention, and 0 recusals.

6. Review from Subcommittee #1

19-095

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, please address the following (see comments below):
    i. Line a, change to 120 for one source or 360 for three sources. As 60 females are mated and 60 are not mated per 2 clones.
    ii. Line b, change to 30 for one source or 90 for three sources as breeders for 60 females for two clones.
    iii. Line c, change to 96 for one source or 288 for three sources as only 16 females are allowed to deliver per 2 clones.
b. In Form A, item 5c, remove IVIS and location as this will not be conducted in live animals.
c. In Form A, item 7d2, please correct justification to #2 or #3 for first two compounds and under MSC please correct stariled.to sterile
d. In Form A, item 8a, please clarify the reference here and in A8g to 3 sources of MSC. Is this a mixed population of cells as there are only enough animals

justified to test cells from one source? If 3 different sources will be tested independently this

e. In Form A, item 8b and 8c, please clarify that the primary goal is to access efficacy of MSC in restoring fertility post-CTX.
f. In Form A, item 8g, please address the following:
    i. Under summary, clarify the 3 sources of stem cells. It is understand that 2 clones will be tested, but is is not clear if those clones will be from different sources.
    ii. Under CTX, please clarify the percent infertility that is anticipated with this method. Is it 100%?
    iii. Under surgery, remove "small" prior to incision on line 6.
    iv. Under experimental design, remove GMP reference as cells cultured in laboratory are not GMP.
    v. Remove justification section as this is part of A8e,
g. In Form A, item 8h, please address the following:
    i. Please change pup number to 24 each as only 4 animals per group will be allowed to deliver.
    ii. Change total females at bottom to 4 and ups to 96.
    iii. Clarify if this study will be repeated for each source of MSCs indicated.
    iv. Please provide a rationale (see A8h instructions) for the group sizes for each time point.
h. In Form A, item 13c, please start this section with the following: Dorsal approach is an alternative to laparotomy and that lab has found ventral approach preferable. Remove last sentence.
i. Assurance page, PI must sign.
j. In Form B, item 6b, please add that prep is repeated 3 times.
k. In Form B, item 6c, move monitoring anesthesia until animals are conscious to end of description.

19-097

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, it is suggested to fill item 2b.
b. In Form A, item 8g, please address the following:
    i. When histatins drops will be administered to mice post-surgery is not clear.
    ii. It is not clear if anesthetics are used for applying eye drops to mice. If so, indicate drug, dose and route. If not, please indicate that animals are manually restrained for eye drop administration.
    iii. Please include that PBS will used as a vehicle for histatins eye drops.

iv. In the second paragraph, please change: 'subconjunctival injection is performed at days 2 and 8' to 'subconjunctival injection is performed at days 2 and 8 post-corneal suture placement'.\In 4th paragraph, it is suggested to either include the details for Ref#24 in the reference list or remove it.
v. In 5th paragraph, it appears that three histatins are being used. Please include the names of the three types.

c. In Form A, item 14, please address the following:
   i. Please clarify who will be performing subconjunctival injection and their expertise with this procedure.
   ii. Remove the procedures/expertise that are not involved in the current protocol.
   iii. Remove [redacted] as trainer as she is never conducted this procedure and clarify who will provide training on this procedure.
   iv. Personnel must update ACC Regulatory Training by updating online course.
d. In Form B, item 7, provide information for subconjunctiva injection and monitoring for any complications.

19-098

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 5a, and remove comments next housing locations.
b. In Form A, item 5c, please address the following:
   i. Please remove lines 5 and 6.
   ii. Line 4, correct location for euthanasia.
c. In Form A, item 7a, uncheck yes and check no for rDNA and remove the IBC number, BSL and lentivirus, as this is done ex vivo.
d. In Form A, item 7c, correct locations
e. In Form A, item 8b, change all references after first sentence from KDM5A to RBP2 as RBP2 mice are requested. Nomenclature needs to be consistent.
f. In Form A, item 8g, please address the following:
   i. Under IP injection, please clarify whether or not cisplatin is pharmaceutical grade. If NPG or formulation is changed for administration to mice, then it must be included in A7d2 and all question answered.
   ii. Under monitoring of tumors method 1, please clarify the criteria that increases monitoring from every other week to weekly. Please reconcile this with monitoring listed in other sections.
   iii. Under Monitoring of tumors method 3, please include dose, volume and route of administration for luciferin under IVIS description.
   iv. Remove the last paragraph prior to description of pilot study: "Procedures to…sacrificed."

v. Under part I and part II, please address the following:
    1. Please verify that the cell have never been passaged through mice. If they have, then check yes for A7b, complete biologic form. NOTE: Murine pathogen tests results will be required prior to use of the cells.
    2. Indicate route of administration for CPI-455.
    3. Specify the method of euthanasia of pregnant mice for isolation of ESCs and MEFs.

g. In Form A, item 8h, please address the following:
    i. Include a justification for the number of animals needed for pilot studies See instructions on justification for pilot studies.
    ii. Part 2 of both the pilot and main study and reconcile the numbers with table A4 accordingly.

h. In Form A, item 10a, add CO2 method to the table for breeding colony.

i. In Form A, item 12a, uncheck "Yes" and check "No" for use of anesthetics, analgesics as this is not done for tumor development.

j. In breeding form, PI should indicate the number of breeder females and males for each breeding table and reconcile the numbers accordingly with total numbers and with A4.

19-107

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. Condition of Initiation: Prior to initiation of PDX cell line, test results per UIC Biologic Material policy must be provided and approved by veterinary staff.

b. In Form A, item 4, change youngest age for nude mice to 4 weeks.

c. In Form A, item 7c, change to active scavenging in procedure room. In addition, please clarify isoflurane use in laboratory is with an isoflurane machine. If not, then in A8g, describe all steps to isoflurane use in PI's laboratory.

d. In Form A, item 7d2, change justification to 2 or 3 and clarify how solution is sterilized for osimertinib.

e. In Form A, item 8b, 2nd paragraph, this states that gefitinib will be given, but in letter of response to vet comments, it was specifically stated tht this compound would not be administered. Please remove.

f. In Form A, item 8d, move first paragraph to include in A8e.

g. In Form A, item 8g, please address the followihg:
    i. Aim 1, please address the following;
        1. Background and rationale as this section is redundant of A8b and not needed. Please remove.
        2. Overview, this is inconsistent with the experiments described are for SC administration only. Remove.
        3. Under SC injections, there are no references to imaging in this protocol. If imaging will be done, then add a separate paragraph, describe the type of imaging to be conducted (ie

IVIS, etc.), administration of any compounds for imaging, anesthesia details (drug, dose, route), when imaging will be conducted and at what frequency. In addition, A5c, A7c, and A7d2 should be reconciled for this issue. If imaging is not conducted, remove reference here.

4. Under monitoring and humane endpoints, please address the following:
    a. Please clarify that study endpoint/duration is 25 weeks and remove 25 weeks as a HEC.
    b. UIC weight loss criteria is 20% weight loss minus tumor mass from baseline and not within a week. Please reconcile.
    c. This section states mice will be euthanized under isoflurane anesthesia, but euthanasia section suggest CO2. Please reconcile. Please indicate the secondary method used with isoflurane prior to tissue harvest.
5. Under euthanasia, please address the following:
    a. As described CO2 cannot be used in this manner. Please review guidelines. Also, please reconcile with comments above related to isoflurane use.
    b. Indicate secondary method to be used prior to tissue harvest.
    c. From B3, it appears that PI will be collecting blood via cardiac puncture. If this is the case, then CO2 cannot be used for this purpose. Please reconcile for the method of euthanasia and reconcile with A10a,b, and c.
6. Under proposed expt #1, please clarify the following:
    a. Under drugs and dosing, remove reference to Gefitnib.
    b. It is suggest that PI consider adding the WT cell line to this study as a control. If added, please revise numbers and justification and reconcile with A4 and Ah.
    c. Remove monitoring and HEC as this is redundant.
7. Under proposed expt #2, please clarify the following:
    a. Paragraph #1 change gefitinib to osimertinib.
    b. Under drugs and dosing, remove reference to Gefitnib.
    c. Remove monitoring and HEC as this is redundant.

ii. Under Aim 2, please address the following:
1. Background and rationale as this section is redundant of A8b and not needed. Please remove.
2. Under goal, please remove reference to confirmed pathogen free. MAP testing is not sufficient.
3. Overview, this is inconsistent with the experiments described are for SC administration only. Remove.
4. In table, remove tested pathogen free.

5. Under monitoring and HEC, indicate same as aim 1 and remove all other information.
6. Under euthanasia, see comments above and reconcile.
7. Under expt #1 and expt #2, remove monitoring and HEC as this is redundant.

h. In Form A, item 8h, please reconcile if addition control is added for Aim 1, expt 1.
i. In Form A, item 10a, 10b, and 10c, see comments above and reconcile for euthanasia.
j. In Form A, item 14, PI must complete training prior to approval. Please provide completion dates for UIC specific online training. Reconcile methods of euthanasia with A10 section.
k. In Form B, item 5a, remove check marks.
l. In Form B, item 6d, remove check marks.
m. In Form B, item 9, see comments above and reconcile for study versus HEC. Remove last paragraph.
n. In Biologic Form, HCC lines should NOT be listed here if they were not derived by passage through mice. Please clarify.

19-099

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, provide institutional approval number
b. In Form A, item 7d2, please add H_2O_2 including scientific justification, source, method of preparation and sterilization.
c. In Form A, item A8e, the justification provided is not related to the experiments described in this protocol, please reconcile
d. In Form A, item 8g, please address the following:
    i. Under Aim 1, please address the following;
        1. Include study timeline from wound incision to MRI scanning for aim 1.
        2. It needs to be clear that this procedure is acute and mice will not wake up following the state of the procedure.
        3. Please indicate the following study 1, that PI will provide an update to ACC as to outcome the study and detection of ROS prior to initiation of Aim 2.
    ii. Provide a timeline for aim 2.
    iii. Indicate the proportion of male and female mice for all experimental groups
    iv. Include justification for using different ages of mice for aim 1 & 2 studies.
    v. Hilltop Lab Inc is not a UIC approved vendor for the purchase of mice. This needs to be corrected to Charles River.

vi. PI should include a description for exsanguination under anesthesia followed by perfusion.

e. In Form A, item 10a, add method 5; please see comments above
f. In Form A, item 13b, expand literature search to include combination of search terms including oxidative stress and wound healing and update literature search accordingly.
g. In Form A, item 14, personnel must update ACC Regulatory Training by updating online course.
h. In Form B, item 3, uncheck "Yes" and check "No" for i.p injection

19-086

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 6c, uncheck no and check yes.
b. In Form A, item 7d2, under source, remove answer for AChR and indicate purified in house in RRC.
c. In Form A, item 8a, please address the following:
    i. Line 2, please add (a type of white blood cell) after T-cells
    ii. On line 3, add "by" after suppressed
d. In Form A, item 8f, please change monitoring to 2-3 times per week from every alternative day and change lack of purposeful movement to severe lethargy. Also, weight loss is indicated in B9, but not here. Please include in this section.
e. In Form A, item 8g, please address the following:
    i. Under expt 1a, please address the following:
        1. According to A8c, prevention for this model is complete. Please clarify.
        2. For justification include standard deviation.
        3. Please clarify if males and females are used in equal proportions.
    ii. Under expt 2a, please address the following:
        1. Please clarify the reference to injection of FCA in the thigh. IM injections with FCA should not be conducted. Also volume for IM is too high and should not exceed 20 ul.
        2. Please clarify the reference to injection in the tail. Is this SC in the tail or it is SC at the base of the tail?
        3. Please change pallet to pellet.
        4. For justification include standard deviation.
        5. Please clarify if males and females are used in equal proportions.
    iii. Under expt 3a, please address the following:
        1. Please clarify route of PT as this has been IP in the past or provide a reference to administration IV.
        2. For justification include standard deviation.

3. Please clarify if males and females are used in equal proportions.

iv. Under expt 4a, please address the following:
    1. For justification include standard deviation
    2. Change monitoring to 2-3 times per week from every alternative day and change lack of purposeful movement to severe lethargy

v. Under expt 5a, please address the following:
    1. Please change post-euthanization to post immunization
    2. For justification include standard deviation
    3. Change monitoring to 2-3 times per week from every alternative day and change lack of purposeful movement to severe lethargy

f. In Form B, item 7, change diphtheria to pertussis
g. In Form B, item 9, please address the following:
    i. For EAT, change blood volume to 50 ul.
    ii. For MG, revise to match what is indicated in A8g.
    iii. For lupus models, revise monitoring frequency to 2-3 times per week from every alternative day and change lack of purposeful movement to severe lethargy. Reconcile with B9 for weight loss criteria.

19-090

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. General Comment: Please note we have requested information from Abwiz on their quality control for murine pathogens.
b. In Form A, item 4, please address the following:
    i. Please indicate the specific conditional KO of IL34.
    ii. Please indicate which RAG KO is used.
c. In Form A, item 5a, check yes for use of biohazard room and uncheck no.
d. In Form A, item 5c, please address the following:
    i. Correct location.
    ii. Add biohazard room and add adenoviral administration.
e. In Form A, item 6e1, please move this information to A6d5.
f. In Form A, item 7a, list the adenovirus to be used.
g. In Form A, item 7b, Biologic Form, remove adenoviral vectors.
h. In Form A, item 7d2, please address the following:
    i. The different types of collagen used should be listed on separate lines.
    ii. Add adenoviruses to this section.
    iii. Please clarify if the CFA, IFA, and mineral are sterile.
i. In Form A, item 8a, change ligation to binding.
j. In Form A, item 8b, please address the following:

i. Define PB in the first paragraph.
ii. Under #4, please clarify what is meant by "identified pathway".
iii. Under #5, please clarify the purpose of studying SDC KO, IL34 KO, and Lyse-Cre/IL34 fl/fl mice and define CIA here. Remove references to breeding.

k. In Form A, item 8c, please clarify #4 as this states this will be done. Work listed here is for what was done.
l. In Form A, item 8g, please address the following:
    i. Prior to the start of experiments, please clarify that wildtype referred in all the studies listed are C57BL/6 mice.
    ii. General Comment: Under several sections in the protocol, monitoring, supportive care, etc is included in bold, along with humane endpoints and study duration. The humane endpoints need to be matched with the comments below for B9 and the study duration needs to be corrected in several studies to match the study.
    iii. Under #1, please address the following:
        1. Please ensure this is written in future and not past tense.
        2. Please clarify the reference to rodent anesthetic machine as PI mentions chemical fume hood for scavenging in the laboratory. If PI is using dessicator then remove this reference and clarify how isoflurane is used in laboratory (ie. Please clarify how mice are separated from isoflurane so they are not in direct contact with chemical).
        3. Please indicate that the same scoring system described under #2 is used for this study.
    iv. Under #4, please clarify when thioglycolate is administered in reference to when antibodies are administered to the mice and reconcile the timing of euthanasia between what is listed for thioglycolate and what is listed for antibodies. If these are two different studies, then this must be clarified and the total number of mice reconciled and thioglycolate added to the table.
    v. Under studies 5, 6, and 7, please address the following:
        1. Please state at the beginning of each section that these are in vitro studies only and only naïve mice are euthanized.
        2. Please clarify why the same mice cannot be used to harvest tissues for all three studies and why separate groups of mice are required.
        3. Please clarify the method of euthanasia for these studies.
        4. Study 6, please clarify the references to 15 mice each when table states 10 per study.
    vi. Under study 9, as currently described, this study appears to be an in vitro only study, but the last sentence before the flow chart and table states that mice will be monitored 3 times weekly. If procedure will be conducted on mice prior to euthanasia, this needs to be clearly indicated here. Moreover, the duration of the study and what mice are being monitored for needs to be clarified.
    vii. Under study 11, please address the following:
        1. Please clarify why chicken collagen is used for this study and bovine is used for all other studies.

2. Please clarify the duration of this study. Bullet #4 indicates monitoring up to day 84 and bullet #5 states study ends at day 52. In addition, for other CIA model study ends at day 45. Please reconcile for duration if longer than 45 days provide rationale.

viii. Under study 12, please clarify why the duration is 52 days versus 45 for study 2.

ix. Under study 13, please address the following:

1. Please clarify what the two diets are and what the goal of these diets is.

m. In Form A, item 8h, please clarify if males and females are used in equal numbers and whether any sex differences are anticipated.

n. In Form A, items 13a and 13b, please list PsA model and genetic model, justify both, and conduct literature search for alternatives for these models.

o. In Form A, item 13c, list full date (month/day/year) and clarify 15 years (2004-2019?).

p. In Form A, assurance page must be signed by PI.

q. In Form B, item 9, please address the following:

i. Please ensure monitoring frequency is consistent with what is indicated in A8g.

ii. Under GPI, please address the following:

1. Please indicate the frequency of weighing animals.

iii. Please add that for any model involving injection at the base of the tail that mice which develop severe skin lesions involving any exposure of tendon or bone will be euthanized.

iv. Under PsA, please address the following:

1. Please remove the following: "In the event…weight."
2. Please add the following: "All supportive care and humane endpoints will be the same as GPI model and Clarify the frequency of observation for this model.

iv. For IA model, please change "the guidelines" to "the HEC listed for GPI. Please indicate the frequency of observation.

19-094

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. General Comments: Prior to submission of revisions, please meet members of ACC to discuss hMISTRG studies due to concerns regarding murine pathogens, housing, and logistics.

b. In Form A, item 5c, line 4, please clarify that those mice administered Ad-ONCO will remain in biohazard room as this is a replication competent virus.

c. In Form A, item 7a, please list the specific constructs to be used and uncheck yes and check no for carcinogen.

d. In Form A, item 7b, please complete biologic form and provide IDEXX results on lines that PI has in house.
e. In Form A, item 7c, correct type of scavenging in biohazard room.
f. In Form A, item 7d2, please address the following:
    i. Please clarify the vehicle for antibodies listed in this table.
    ii. Please add AD-Onco+/-Light to this table.
    iii. Please clarify that AD viruses are generated under sterile tissue culture conditions and indicate the vehicle.
    iv. Please clarify the vehicle for luciferin and clarify method of sterilization.
g. In Form A, item 8a, please clarify what CTLA4 is in lay language.
h. In Form A, item 8b, please define TIL in 3rd paragraph and clarify the purpose of LTβR-IgG in this section.
i. In Form A, item 8g, please address the following:
    i. Prior to study description, please clarify if males and females will be used in equal numbers in each group and whether any sex differences are anticipated.
    ii. Under expt #1, please indicate maximum volume of antibody injected and clarify that this is the same for all other expts.
    iii. Under expt #2, please address the following;
        1. Please add (See Form B for surgical details) after splenic injection on line 5.
    iv. Under expt #4, please revise "when the largest tumor size reaches 2 cm" to "when total tumor diameter reaches 2 cm".
    v. Under expt #5, please correct volume of antibody administered.
    vi. Under expt #7, please indicate the dose of ketamine and xylazine.
    vii. Under expt #10, please clarify that matched means patient matched.
    viii. Under expt #11, please clarify when in reference to SC tumor inoculation animals will be shipped to UIC as treatment starts on day 6.
    ix. Under expt #12, please clarify if intrasplenic surgery will occur at UIC or collaborator's institution. Please contact ACC to discuss the logistics of this study.
    x. Under MRI, please add that animals will be continuously monitored until recovered from anesthesia.
    xi. Under IVIS and ultrasound, please add that animals will be continuously monitored until recovered from anesthesia and in second sentence, change left to right lower quadrant.
    xii. Regarding imaging, please clarify the maximum frequency at which IVIS, MRI, and US will be conducted for this expt.
    xiii. Under IV injections, please address the following;
        1. Remove "As per…node/37).
        2. Regarding RO, remove "and gently,,,head," this is not for injections.
j. In Form A, item 14, please remove reference to protocol 13-224 and indicate ~ 6 years of experience.
k. In Form A, assurance page needs to be signed by PI.
l. In Form B, item 6c, please address the following:

i. Remove the paragraph on tumor implantation of tumor fragments. This procedure is not part of this protocol.
ii. Reconcile weighing frequency with what is listed in A8g.

m. In Form B, item 9, please address the following:
i. For experiments #3, 4, 5, and 11 in which treatment will be administered intratumoral route, please clarify if any ulceration at the site of injection is anticipated due to treatment effect. If so, then please clarify humane endpoint for those studies to indicate ulcerated tumors in which ulceration is not at the site of injection.
ii. In paragraph 4, please revise "when the largest tumor size reaches 2 cm" to "when total tumor diameter reaches 2 cm".
iii. In paragraph 5, change body to muscle.
iv. Indicate the frequency of weighing animals and ensure this is consistent with A8g.

l. In Hazard form, please indicate the handling procedures for IVIS, MRI, and ultrasound. Contact ACC to discuss prior to submission of revisions.

19-105

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, please reconcile number estimates with A8h.
b. In Form A, item 8b, paragraph #2, please add "and ADME after Pharmacokinetics.
c. In Form A, item 8e, reconcile the strains that are listed here with what is listed in A4.
d. In Form A, item 8g, please address the following:
i. Define ADME in experimental design under 'Rats'.
ii. Injection volume for mice is too high for IV as this would be 300-600 ul. Please revise.
iii. Please clarify for jugular cannulated rats if animals are cannulated with external catheters, pin ports or vascular access buttons.
iv. Under repeat dose, please clarify the reference to single dose.
e. In Form A, item 8h, based on the description for number of animals required, the total number that is anticipated is not 1200. Please reconcile.
f. In Form A, item 14, the training dates for the personnel should be updated
g. In Form A, item 15, PI signature should be included.

19-108

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed

to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 6d, please rewrite this section to indicate the following and remove current answer: "Due to the need for multiple personnel and space in housing rooms, glucose/insulin tolerance tests and fasting measurements will take please in PI's laboratory and in order to ensure that animals are acclimated prior to the testing, animals will be fasted and tests conducted in lab. The total duration of time in the laboratory is X hours." In addition, please clarify that for pyruvate animals, fasting will be initiated in animal facility and that animals will not be removed from animal facility until later in the day and no animal will be in PI's laboratory beyond maximum time indicated above.
b. In Form A, item 7a, please indicate IBC and remove BSL2.
c. In Form A, item 7d2, please address the following:
    i. Please clarify that AAVs are prepared in an aseptic manner.
    ii. Please clarify the method of sterilization for STZ.
d. In Form A, item 8g, please address the following
    i. Under segment #1, expt #1, please clarify the reference to blood being collected via decapitation as multiple blood samples are collected per animal.
    ii. Under 1b, expt #3, please remove reference to IPGTT "as described above" as this is described at the end of A8g.
    iii. Under IIa1, expt #1, please clarify biweekly- twice per week or every other week?
    iv. Under IIb, Genetic T1D, remove using T1 FFAX mice as this the the STZ model.
    v. Under IIc, please clarify that these studies will be conducted as terminal studies with mice euthanized at the end of sampling.
    vi. Under IIIa, please clarify what SCFA is.
    vii. Clarify the specific studies/expts that involve decapitation of animals without prior anesthesia.
    viii. General comment, other than isolation of islet cells, it is not clear why tissue harvest of any other organ must be conducted as an acute surgical procedure. Please justify for specific studies why this must be done. If these tissues can be harvested post-mortem, then in A8g correct in all applicable sections.
    ix. Under methods, for pyruvate tests, please justify why fasting for 24 hours is required. Please clarify the frequency at which this procedure is conducted and if combined with other fasting methods for the same group of animals, time lines must be clear as to how many fasting intervals and their length individual animals undergo.
e. In Form A, item 10a, line 1, column #3, remove answer.
f. In Form A, item 12b, check yes.
g. In Form A, item 13a, see comment above regarding acute tissue harvest and justify genetic T1D model.
h. In Form A, item 14, please address the following:

i. Please verify that personnel #8 is still conducting all of these procedures under this protocol and correct training dates to 10/30/17 for both training.
ii. Please verify that personnel conducting decapitation without euthanasia and indicate that personnel will demonstrate proficiency to a member of the veterinary staff for this method.

i. In Form B, item 8a, add shaving for acute islet harvest.
j. In Form B, item 6c3, surgery 2, see comment above related to acute harvest and reconcile.

7. Review from Subcommittee #2

19-089

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 5 in favor, 0 opposed, 0 abstentions, and 2 recusals.

a. In Form A, item 7d2, please add Dulbecco's Phosphate Buffered Saline.
b. In Form A, item 8a, please clarify "abnormal Alpha synuclein" in the first sentence. What does this mean? Abnormal levels? Abnormal formation?
c. In Form A, item 8b, there is reference regarding the intragastric administration route in rodents for testing this mode of transfer. Please clarify why this route would not work for this species, as it seems to be less invasive.
d. In Form A, item 8g, please address the following concerns:
    i. Please clarify the time line for euthanasia. Is it 6 or 12 months post- surgery? 6 months is indicated in the table and 12 months is indicated under clinical rating and euthanasia. Please reconcile.
    ii. Under CSF and blood collection, lease remove the last two sentences staring with "Due to the small CSF collection volume …in previous studies."
    iii. Under abdominal surgery, please address the following:
        1. Please indicate that cefazolin will only be given once post-surgery and remove BID for 5 days.
        2. Please add Ondansetron 0.2 mg/kg IM once post-surgery and as needed for nausea.
        3. Under clinical rating, protocol indicates that no impairments were previously seen when α-syn PFFs was adminitered in the gut at up to 12 months post-surgery, and that any deficits seen in this study are anticipated to be very mild. Please clarify why this is expected.
e. In Form A, item 13b, conduct search for alternatives to abdominal laparotomy.
f. In Form A, item 13c, laparoscopic surgery is an alternative that should be listed here and PI should indicate that open laparotomy is the preferred method to ensure injection into the appropriate site in the gut.
g. In Form B, item 6c, surgery 1, please address the following:

i. Please indicate that cefazolin will only be given once post-surgery and remove BID for 5 days.
ii. Please add Ondansetron 0.2 mg/kg IM once post-surgery and as needed for nausea.

h. In Form B, item 6f2, please add Ondansetron 0.2 mg/kg IM once post-surgery and as needed for nausea.

19-106

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 8e, 2nd paragraph, please remove the reference to gender–specific difference and justify why only female mice will be used.
b. In Form A, item 8g, please address the following concerns:
    i. Please change the word "scuffing" to "scruffing" in the entire protocol.
    ii. Please indicate that sterile gloves will be changed in-between each cage change.
c. In Form A, item 14, personnel must update ACC Regulatory Training by updating online course.

19-046

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, please reconcile the animal numbers based on experimental aniamls in A8g and breeding tables.
    i. Change the numbers to following: 4a: add the 20 experimental animals, 4c: change 20 to 40 for experimental animals, 4f and 4g, change 10 to 20 experimental animals.
    ii. 40 wild type mice should be added for AOM/DSS model.
b. In Form A, item 8b, please define the following acronyms: CRC, DSS and AOM.
c. In Form A, item 8f, 4th line please change the "greater than 15% gain or loss of body weight" to the following "15% gain in body weight and abdominal distension".
d. In Form A, item 8g, please address the following:
    i. In AOM/DSS model, please clarify the strain of WT mice.

ii. Please clarify if the goal is to assess tumor growth rate and compare then between KO and non-KO for the two models or compare tumor burden. Growth rate would suggest that study endpoint would equal the time as which animals reach humane endpoints. Tumor burden would suggest that PI should euthanize all animals at the same time once tumors develop to compare burden at a specific time. If the goal is growth rate, then please clarify the maximum duration for each model. If the goal is tumor burden, then clarify for each model, at what point animals will be euthanized.

e. In Form A, item 9, for dead animals, please check an option (freezer, refrigerator or discard).
f. In Form A, item 12a, 2nd part please check "No".
g. In Form A, item 13a, please justify why both models are needed. Also clarify that carcinogen-induced model is the same as chemical induced model as written in 8a.
h. In Form A, item 13b, there are too many search terms for an earnest search .
i. In Form A, item 14, personnel must update ACC Regulatory Training by updating online course.
j. In Form B, item 3, please address the following concerns:
    i. Under collection of biological samples, please uncheck "No".
    ii. Under Tail Snip, "Yes" box is checked but anesthetic is not listed, please reconcile.
    iii. In Form B, item9, first sentence should be changed to the following: 15% gain in body weight and abdominal distension.
k. In Breeding Form, please provide an answer to item 4.

19-092

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form B, item 5b, please provide an answer regarding justification for multiple survival surgeries conducted at different surgical settings. If there is a chance that a pump would be inserted and later removed and/or removed and replaced, then the multiple surgeries for this issue must also be justified.
b. In Form B, item 6c, surgery #1, under telemetry implantation, page 5 of 11, for skin closure suture pattern change "continuous and intradermal to "continuous or intradermal".
c. In Form B, item 6c, surgery #2, please address the following:
    i. Please indicate the specific model number for the pump listed and the duration that the osmotic pump lasts.
    ii. See comments above related to surgery for pump removal and/or removal and replacement and address those procedures here in separate paragraph.

8. Review from Subcommittee #3

19-075

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, please see comments below and reconcile numbers with A8g.
b. In Form A, item 7c, should be completed for the use of isoflurane in [redacted] and active scavenging should be indicated.
c. In Form A, item 8c, define DSS the first time used in the protocol.
d. In Form A, item 8g, please address the following:
    i. In summary analysis and numbers associated with specific projects, please reconcile the number of animals proposed between the respective sections. A4 lists 480 B6 and 80 Nrf2 KO mice and this section under summary analysis indicates the need for 420 animals for a three-year period, and the number of animals listed for each of the 4 projects totals 224 animals. All numbers need to be congruent.
    ii. On page 1 of 7, 1st sentence remove reference to "Project 5".
    iii. On page 1of 7, this states exposure for 5-7 days, but A8c, indicates that it was determined that exposure for 7 days was optimal; therefore, either correct here, or provide rationale as to why a range is still being proposed.
    iv. Under the Blood/Plasma/Serum section, the protocol indicates experience with various blood collection techniques except for RO blood collection implying that the PI does not have experience with this technique. For consistency, please clarify experience with the technique. In addition, under this section, please clarify euthanasia method. It does not seem logical to have animals under isoflurane anesthesia and then to move them to a CO2 chamber for euthanasia. This process should be reconsidered. See comment for A10aa below.
    v. Page 2 of 7 since weight is being used as an endpoint criterion, please indicate the frequency with which weight will be assessed during the study.
    vi. Projects 1-4, indicate the specific line of mouse to be used for each project.
    vii. Project 1, please address the following:
        1. In the first paragraph, colon cancer cells are referenced; however, it would appear that this study is focused for IBD. Please clarify.
        2. Under expected results (page 3 of 7), the time line proposed here are not consistent with the first paragraph of A8g or

with what is stated in A8c. A8g 1st paragraph, indicates 5-7 days of DSS and A8c indicated that 7 days has been determined to be optimal. This also does not match the timelines provided at the end of the study. Please reconcile all sections.

3. Under expected results, it is not clear if the duration of the diterpenes treatment. Under oral dosing, administration for 5-7 days per week is indicated, but it is not clear under project 1 if the administration of diterpenes will continue after pre-exposure and for how long. This also doe not match what is in the time line. Please reconcile differences.

viii. The titles for projects 1 and 3 are the same (anti-inflammatory studies); however, the study time-lines are different please clarify.

ix. Provide a project time line for project 4 on the last page of this section.

e. In Form A, item 8h, remove the last sentence from the justification paragraph: "This was performed in consultation".

f. In Form A, item 10a, consider including exsanguination or cervical dislocation under isoflurane anesthesia as it would appear that most animals will be under isoflurane anesthesia at the time of terminal blood collection.

g. In Form A, item 13a, the second sentence of this section places an emphasis on cancer development; however, this project appears to be focused toward IBD. Please clarify.

h. In Form A, item 14, please address the following:

i. Correct PI's training dates to 8/31/18 for ACC Regulatory training and 10/31/14 for Mouse/Rat/

ii. Some personnel must update ACC Regulatory Training. Training must be updated every 3 years and completed prior to protocol approval.

iii. Please indicate specifically who will be responsible for providing special diets and water with test agents.

i. In Form B, item 7, please remove the last sentence in this section. Indicate how often the animals are observed while on DSS and what clinical signs the lab is monitoring for sick animals and the course of action that will be taken if animals do become sick.

19-100

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. Condition of initiation: Prior to initiation of the project (at least 90 days), the PI must discuss the feasibility of housing these rats and the use of behavior equipment with veterinary staff as these animals come from a colony with microbial agents excluded from the UIC rat colonies.

b. In Form A, item 3, please address the following:
    i. Please list the title of the grant.
    ii. Please move the grant number to item d.
    iii. Please add institutional number for PAF
c. In Form A, item 8g, please address the following:
    i. Expt. 2 this section indicates the use of pentobarbital anesthesia for placement of brain cannulas; however, in B4 and B6, protocol refers to the use of isoflurane. Please reconcile.
    ii. Expt. 2 under the description of the perfusion technique provide more information on the procedure, (i.e. is access to the heart gained through the abdomen or the chest wall, how depth of anesthesia is assessed prior to perfusion and the approximate duration of the procedure.)
    iii. Expt. 3 under alcohol preference remove reference numbers 40 and 79.
d. In Form A, item 8h, please address the following:
    i. The alcohol preference rats in A8g for expt. 3, do not appear to be described/accounted for in the table. Please include.
    ii. Last paragraph of this section justifies 8 animals per group for alcohol preference yet in A8g and in the table in A8h, 7 animals per group are listed. Please reconcile the difference.
e. In Form A, item 13a, the painful procedures conducted in this protocol need to be listed here and justified. This would include stereotaxic cannula placement.
f. In Form A, item 13b, list the period of years searched.
g. In Form A, item 13c, if no alternatives were found then answer should be removed from this section.
h. In Form A, item 14, provide detailed information as to [redacted] experience with the techniques he will be performing in this protocol and clarify in this section for all staff listed who will be performing the surgery, behavior tests, alcohol preference test and the proposed euthanasia techniques.
i. In Form B, item 6c, clarify if the cannulas obtained from the company are sterile at the time of purchase. If not, then they need to be sterilized via ethylene oxide at the [redacted].

19-101

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 5c, PI's laboratory is listed for experimental purposes. If experimental purposes refers to in vitro experiments, then remove reference to room and building number. If euthanasia or IP injections will be conducted in PI's laboratory, then indicate these specific procedures. NOTE: currently, protocol indicates that IP injections and euthanasia will be done in [redacted] and an

approved CO2 station inspected by the veterinary staff would be required in the PI's laboratory.

b. In Form A, item 13b, please indicate the specific number of relevant references for the respective literature searches.

19-093

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review by a subcommittee of members 6 and 10 for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, provide a copy of the COI grant to match to this protocol.
b. In Form A, item 5d, check no.
c. In Form A, item 7a, for biohazard, uncheck yes and check no as animals will not be housed differently.
d. In Form A, item 7c, please address the following:
    i. List room 118, isoflurane and active scavenging.
    ii. List room 186c and discuss the use of isoflurane with veterinary staff prior to submission of the revision.
e. In Form A, item 7d2, E2 and preparation needs to be listed in this table with gamma irradiation for sterilization of these implants.
f. In Form A, item 8b, please CDX first time used.
g. In Form A, item 8g, please address the following:
    i. In table, please address the following:
        1. Please clarify the vehicle group. Is this a vehicle for Fulvestran IP or the vehicle for NSEs via gavage or both?
        2. Clarify which NSEs are SERDs and which are bromodomain inhibitors. NOTE: PI must ensure that the NSE number assigned for a compound is consistent throughout the protocol and any modifications so that it is clear which compound is being used or requested.
    ii. Under stereotaxic injection of human breast cancer cells, please clarify the following:
        1. The first paragraph references to "percutaneous injections", but in B6c, the protocol specifically references to bregma coordinates, which cannot be visualized without conducting a skin incision to visualize the skull. Please verify whether this procedure will be conducted percutanously or if it will be done via surgical cutdown and reconcile here and in B6. If done percutaneously, provide a reference in mice to this specific procedure for injection into the ventricle.
        2. In second paragraph, change "human" endpoint to "humane" endpoint.
    iii. Under treatments, please indicate the doses to be administered for the various NSEs in mg/kg, the maximum volume to be administered, and when treatment is initiated.

iv. Under slow release capsules implantation,
    1. Please move preparation to A7d2 as indicated above.
    2. Provide the rationale as why E2 is being used and whether it is required for both cell lines listed in the table.
    3. Please clarify the size of the implant and why the incision is so large. The subcutaneous pocket can be larger than the skin incision.
v. A section on monitoring frequency and humane endpoint criteria need to be added to this section.

h. In Form A, item 8g, please address the following:
    i. As there are 11 groups it is not clear what "pairwise" comparisons are being conducted. Multiple t-tests are not appropriate. Please clarify the statistical analysis to be conducted and indicate the effect size used for determination of sample size.
    ii. Remove reference to both models as only one model is described in the protocol.
i. In Form A, item 13a, please list stereotaxic surgery for administration of cells and SC surgery for administration of E2 and justify both.
j. In Form A, item 13b, please conduct literature search for alternatives to continuous E2 administration.
k. In Form B, items 5a and 5b, if surgery #1 is not percutenous, then check multiple survival and provide a justification as to why E2 implant surgery take place 48 hours prior to stereotaxic surgery.
l. In Form B, item 6c, surgery #1, please address the following:
    i. Please indicate the first dose of anesthesia is administered prior to start of the procedure.
    ii. Indicate how depth of anesthesia is assessed.
    iii. See comments above related to percutaneous administration and provide a reference as to this specific procedure being conducted percutaneously and remove references to bregma coordinates as these cannot be visualized for percutaneous administration.
    iv. If skin incision and burr holes are drilled, provide all of the details regarding these procedures and how drill bits are sterilized and include details of wound closure and when sutures or wound clips are removed.
    v. Indicate the duration of the procedure.
m. In Form B, item 6c, surgery #2, please address the following:
    i. Please clarify the size of the implant and why the incision is so large. The subcutaneous pocket can be larger than the skin incision.
    ii. Indicate duration of the surgery.
    iii. Indicate when surgical staples for the E2 implant are removed.
n. In Form B, item 9, please add seizures, obtunded or circling behavior as additional humane endpoints.

19-103

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. General Comment: Remove MWM from A5c and remove all references in A8g to dry land version.
b. In Form A, item 4, please ensure numbers are reconciled with comments below.
c. In Form A item 6c, the second part of this question needs to be answered.
d. In Form A, item 7d2, include artificial CSF in table.
e. In Form A, item 8g, please address the following:
    i. Under study design last paragraph, remove reference to animals receiving ad lib food as animals will be food restricted on this protocol.
    ii. Indicate the disinfectant that will be used to clean cheese board apparatus.
    iii. For each experiment involving food restriction, please indicate the maximum duration of the food restriction.
    iv. At the end of experiment 3 and 4 it is indicated that a total of 72 rats per study, but according to the text and table 1 at the end, there should be 96 rats/experiment.. Please reconcile.
f. In Form A, item 8h, please address the following;
    i. Change ACC# from 16-103 to 19-103.
    ii. Clarify total number of animals needed – in this section 290 is indicated, but in A4 and A8g, 288 animals are listed. Please reconcile.
g. In Form A, item 10a, the use of ketamine and xylazine as an euthanatizing agent the dose administered needs to be 5 times the standard dose; therefore, dose must be 500mg ketamine and 50 mg xylazine.
h. In Form A, item 13b, last column of table, remove answer and list Yes.
i. In Form A, item 8g, and in Form B item 6b and 6c, reconcile the amount of additional anesthesia that will be administered (i.e. is it 25 or 50 % of the original dose as the percentage varies between sections).
j. In Form B, item 10, please clarify if food restriction is maintained during PSG and subsequent behavioral testing on the back end of the experiment. For each experiment, indicate the maximum number of days that the animals are food restricted.

9. Designated Review(s), Exemptions, and Lab Visits

a. Protocols

There were none this month.

b. Exceptions

Member 6 directed the Committee's attention to the following protocols requesting continuation of partial exemptions from the UIC Environmental Enrichment Plan this month. Following discussion that continuation of the partial exception was appropriate, a motion to approve continuation was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

18-115- The PI of this protocol has requested a partial exemption from the UIC Environmental Enrichment Plan. More specifically, the PI has requested exemption from social contact through pair or group housing and food supplements to minimize the potential of acquiring an infection while the animal is in an immunocompromised state. In terms of food supplements, special caution is needed during the post-transplant period. In this case animals will receive only soft processed food from sealed containers, as well as fruits and vegetables which are clean and immediately after removing the skin in the case of bananas.

c. Lab Visits

Member 6 informed the Committee that the following labs were visited as part of the post-approval monitoring program.

Lab	ACC
[redacted]	18-240
	19-019
	16-144, 16-157, 17-081, 18-024
	16-162, 17-021, 17-192, 17-195, 18-144, 18-239, 19-004
	17-221, 17-222
	17-073, 18-030, 18-121
	17-096
	17-137, 18-204

10. New Business

a. Update of ACC Policy

Member 2 directed the Committee's attention to the updates for photography, videography, and cell phone use in animal facilities. The Committee discussed the following: that animal facilities should be changed to "of animals", that examples should be added for items that require prior approval, and that "or as posted" should be added to areas where phones, electronic, devices, and headphones use is not allowed. Following discussion, a motion to approve the updated policy with the above corrections was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

b. Review of Euthanasia Policy

Member 2 directed the Committee's attention to the euthanasia policy for review. The Committee discussed that the policy was updated for format and links and that no additional changes were needed at this time. Following discussion, a motion to approve the updated policy was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Review of Major Multiple Survival Surgery Policy

Member 2 directed the Committee's attention to the euthanasia policy for review. The Committee discussed that the policy was updated for format and that no additional changes were needed at this time. Following discussion, a motion to approve the updated policy was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

d. Protocol 19-114

The Committee reviewed the protocol and discussed that the purpose of this study is to determine the role that obesity and oxidative stress plays in atrial fibrillation susceptibility. The Committee discussed the following: that there were discrepancies in diet description in the VA protocol that needed to be addressed, that animals on food restriction would require single housing, cage labeling for fasting and maintenance of a log, that the training dates needed to be corrected or updated, that locations needed to be corrected, that numbers needed to be revised to match corrections in VA protocol, and that scavenging in PI's lab for isoflurane needed to be clarified. Following discussion, a motion that the revised protocol needed to be submitted for designated review determination was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

e. Modification of Protocol 18-213 (01)

The Committee reviewed the request for a change in PI to a research associate professor who is currently on the protocol and will be taking over the project due to the death of the former PI. The Committee discussed that funding agency had been notified and the new PI was well qualified to conduct the project. Following discussion, a motion to approve this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

f. Modification of Protocol 19-010 (01)

The Committee reviewed the request for a change in PI to a research associate professor who is currently on the protocol and will be taking over the project due to the death of the former PI. The Committee discussed that funding agency had been notified and the new PI was well qualified to conduct the project. Following discussion, a motion to approve this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

g. Modification of Protocol 17-061 (16)

The Committee reviewed the PI's request for use of two animals to test lower doses of [redacted] at 4 and 6 mg/kg IV due to toxicity seen at higher doses to determine the MTD for future GLP studies. The Committee discussed the following: the doses for rats needed to be corrected, that the vehicle needed to be clarified, that the efficacious dose and dose equivalent needed to be indicated, that a vehicle only group should be added and the flow of the study for groups needed to be clarified. Following discussion, the consensus was that the revised modification should be sent to the Committee for designated review determination.

h. Modification of Protocol 19-008 (01)

The Committee reviewed the PI's request for the following: 1) Addition of 270 for expts (340 total) CD11cCre/PPARg fl/fl mice for LPS, PA, or TBI/bone marrow transplant/LPS studies, 2) Addition of 180 for expts (247 total) Cdh5Cre-ERT2/Csf1 fl/fl mice for LPS and PA studies, 3) Addition of 90 CX3CR1CreERT2/R25tdTomato/CXC3CR1gfP mice for LPS and PA studies (100 total), 4) Addition of 9 CX3CR1CreERT2 :R26 tdTomato/+ as bone marrow donors, 5) Addition of 45 per strain (WT mice, CCR2ko, CX3CR1gfp/+, CX3CR1CreERT2/+:Csf1R fl/fl, Csf1R fl/fl, Lys2CreERT2 :R26 tdTomato/+, and CX3CR1CreERT2 :R26 tdTomato/+ for PA studies (360 total with breeding). 6) Addition of PA and TBI/TSI/bone marrow transplant models. The Committee discussed that the PI needed to clarify donor to recipient ratio and that studies included both TBI and TSI, correct total to 360 for D5b, including monitoring frequency and criteria for PA model, method of euthanasia for donor animals, and include hazard form. Following discussion, a motion that clarifications were needed with designated member review following full committee review for this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

i. Modification of Protocol 19-039 (01)

The Committee reviewed the PI's request for tumor resection in mice with SC Prostate cancer cells in order to continue to follow the mice for tumor metastasis. Following discussion that the PI had provided appropriate rationale for this study and appropriate description of the study, a motion to approve this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

j. Modification of Protocol 18-011 (06)

The Committee reviewed the PI's request for a second thoracotomy surgery for administration of iPSC at 72 hours post I/R surgery and addition of personnel. The Committee discussed that the PI needed to address the following: justify the rationale for the second surgery and the timing of the surgery, clarify specifically what needs to be evaluated on echo to determine of animals will be used for cell injection, conduct a pilot

to determine morbidity and mortality of this procedure at UIC, provide reference, and rewrite the surgical description flow. Following discussion, a motion that significant clarifications were needed and to defer the modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

k. Modification of Protocol 17-117 (01)

The Committee reviewed the PI's request for 54 C57 mice to add periodontal ligament ligation +/- treatment with CD24Fc to the protocol. The Committee discussed that the PI needed to clarify dose of CD24Fc to be used for pilot study, use a non-treated ligation as control, and what percentage reduction in inflammation would be considered successful to continue the study in the pilot, remove references to biohazards, complete literature search for alternatives, and correct funding information. Following discussion, a motion that clarifications were needed with designated member review following full committee review was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

ANIMAL CARE COMMITTEE MEETING MINUTES
JULY 16, 2019

Attendees: Member 2, Member 6 Member 8, Member 9 (arrived late), Member 10, Member 11, Member 24, and Member 30

Absent: None

Guest: Member 39

1. **Minutes**

Minutes were sent for designated review determination.

2. **Announcements**

None

3. **Old Business**

a. Modification of Protocol 17-061 (10)

The Committee reviewed the PI's request for use of 1 animal to test M3mP6 in micelle formulation using TFA salt formulation at bolus of 0.417 mg/kg followed by a second bolus dose of 4.17 mg/kg, infusion, followed by 10 mg/kg/day 24 infusion. The Committee discussed the following: that the PI was requesting to administer two bolus doses, 0.417 and 4.17 mg/kg, to be administered one hour apart followed by 24 hour infusion at 10 mg/kg/24 hours. The Committee discussed that the PI needed to provide animal numbers in the table, and remove references to old and new peptides and use the description of source instead and The Committee also discussed the following: that the TFA formulation of the peptide had been tested in rats without adverse effects and that the same formulation had been tested in dogs in skin test without adverse effects, that the compound would be administered at a low bolus dose with one hour washout a higher bolus dose and then 24 hour infusion with the lost tested for skin and the same peptide formulation tested in rats, and that following testing, PI needed to provide update on results to ACC. Following discussion, a motion that clarifications are needed with designated member review following full committee review via subcommittee of members 2 and 6 for this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstention, and 0 recusals.

Member 9 arrived

b. Modification of Protocol 17-061 (16)

The Committee reviewed the PI's request for use of two animals to test lower doses of IS-003 at 4 and 6 mg/kg IV due to toxicity seen at higher doses to determine the MTD for future GLP studies. The Committee discussed that PI needed to do the following: clarify if the vehicle alone that is proposed in this modification had been tested in rats and if not, than conduct this study first, provide copies of the data on vehicle, 100 mg/kg and 200 mg/kg in rats using the same vehicle proposed in this study with no adverse effects, and indicate the veterinary will be present when dosing is initiated. The Committee also discussed that it was now clear now that the estimated efficacious dose in this species was significantly below the MTD being tested, that a vehicle only group had been added, and that the flow of the study for groups was clarified. Following discussion, a motion to approve this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstention, and 0 recusals. Following discussion, a motion that clarifications were needed with designated member review following full committee review via a subcommittee of members 2, 6, and 10 for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Modification of Protocol 18-011 (06)

The Committee reviewed the PI's request for a second thoracotomy surgery for administration of iPSC at 72 hours post I/R surgery and addition of personnel. The Committee discussed that the PI needed to address the following: that the reference provided was not for two thoracotomies as the treatment but rather was via intracardiac puncture IV treatment which is a potential refinement, complete the surgical description, and that PI needed to address why this method could not be used, that the PI would conduct a pilot study to determine feasibility and provide feedback to the ACC the following: mortality after first surgery, number of surviving animals that meet ejection fraction criteria for cell administration, and morality after second surgery within one week of surgery, and that the PI needed to complete surgical description include wound closure and chest evacuation. Following discussion, a motion that clarifications were needed with designated member review following full committee review for the modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

d. Modification of Protocol 18-095 (04)

The Committee reviewed the PI's request for Addition of 6 animals for ultrasound and mapping prior to RF and/or cryo lesions. Animal may be maintained up to a maximum of 8 weeks post-lesions and then undergo terminal mapping and ablation. The Committee discussed the PI needed to revise the rationale to include a more detailed accounting of the animals requested and 4 remaining animals. Following discussion, a motion that revisions to this modification would be sent to Committee for designated review determination was passed by the following vote: 8 in favor, 0 opposed, 0 abstention, and 0 recusals.

4. [redacted] Director's Legislative and Facility Update

The Committee discussed the following: 1) Capital Programs selected an engineering and architect firm to develop a plan and cost estimate for an HVAC infrastructure upgrade and that the campus has committed substantial funds to the project, and 2) that the new post-doctoral fellow in laboratory animal medicine has joined [redacted] after completing DVM from UIUC veterinary school and will follow the standard rotation.

5. OACIB

a. Modification

Member 2 updated the Committee to the following activity during the past month: there were 0 modifications approved via administrative level, 27 modifications approved administratively following veterinary consult, and 13 modifications approved via designated review this month. In addition, there were 28 protocols that added personnel, 0 with personnel deletions, 1 that added new funding, and 0 in which animals were added to the holding protocol.

b. Continuations and Terminations

Member 2 directed the Committee's attention to the protocols for continuation and those terminated due to expiration or PI's request. The Committee discussed that all protocols had completed the appropriate continuation documents and a motion for designated member review for renewal the protocols was passed by the following vote: 7 in favor, 0 opposed, 0 abstention, and 0 recusals.

6. Review from Subcommittee #1

19-118

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 1, change to "Protection from Ischemia and Reperfusion Injury in rodent models."
b. In Form A, item 14, please add under trainer and expertise, that PI will be trained by collaborator on perfusion method.

19-119

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, total mice as proposed equal 1026. Please reconcile.
b. In Form A, item 7c, please remove TBD after room number and add [redacted]
c. In Form A, item 7d2, please address the following:
    i. Please include PBS and matrigel.
    ii. In the second column, please use the designations at the end of the table to provide a justification and remove current answers.
d. In Form A, item 8a, please define PPP3CC and PPP2CB at first use.
e. In Form A, item 8d, please clarify where the tissue is coming for ex vivo explants and organoid based studies. Will this be from tumors harvested from the current animals proposed in this protocol?
f. In Form A, item 8g, please address the following:
    i. In the study design please include at what time points animals will be sacrificed and which tissues will be harvested post mortem.
    ii. Under castration, please revise the first sentence to read. Isoflurane will be administered via inhalation and in addition, buprenorphine SR LAB (1.0 mg/kg) will be administered SC.
    iii. Under Intracardiac, please address the following:
        1. Please add 15% weight gain and body condition score of less than 2 to the humane endpoint criteria.
        2. Under anesthesia for bleeding, please address the following:
            a. For tail vein blood collection, remove the reference to needle injection and indicate if needle insertion is not correct, procedure will be attempted at a site more proximal on the tail. Indicate the maximum number of attempts.
    iv. Under experimental endpoints, please remove 'table of transgenic animals to be used'.
g. In Form A, item 8h, please address the following:
    i. Under both SC and intracardiac remove the last bullet point, as the number of animals per line is different due to the different take rates and these numbers are incorrect. Total mice for SC is 534 and for IA is 492.
    ii. injection headings iii) please add if mice lose more that 20 % of their body weight (excluding the weight of tumors) or gain more that 15% body weight or if body score condition decreases to 2 mice will be humanely euthanized.
h. In Form A, item 14, clarify expertise for submandibular blood collection or indicate who with expertise will train PI.
i. In Form B, item 6c, surgery 1, please address the following:
    i. Isoflurane will be administered via inhalation and in addition, buprenorphine SR LAB (1.0 mg/kg) will be administered SC.
j. In Form B, item 6e, move castration to Class 2 surgery and check appropriate box for analgesia. Remove information under class 3.
k. In Form B, item 9, match this section with A8g and list humane endpoint criteria for IA model that are consistent with A8g.

19-123

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. Condition of Initiation: Provide copies of murine pathogen testing to ACC and approval from veterinary staff prior to initiation of any of the tumor lines listed in Biologic Form.
b. In Form A, item 4, please address the following:
    i. Line a, this should be 160 (see comments below).
    ii. Line c, this should be 160 (see comments below).
    iii. Line g, add Balb/C and 80 mice (see comments below).
c. In Form A, item 5c, please address the following:
    i. Line 2, remove oral gavage as this is not part of this protocol.
    ii. Line 5, add Adenoviral injections to biohazard room procedures.
d. In Form A, item 7c, please add IVIS location here and active scavenging for this location.
e. In Form A, item 8g, please address the following:
    i. Under General Mouse Husbandry, please address the following:
        1. In 1st paragraph, line 3, remove [redacted], as any mice from [redacted] must be moved to [redacted].
        2. In 4th paragraph, remove the 2nd sentence.
    ii. Under both SC and MFP tumor implantation, please add "minus tumor mass" to 20% weight loss criterion and add 15% weight gain.
    iii. Under adenoviral administration, RO route is listed, but then section refers to experience with tail vein. Please clarify.
    iv. Under primary tumor resection, in the second paragraph, line 3, change tumor bearing mice to "Mammary-fat pad tumor bearing mice…".
    v. Under tail vein injections, add 15% weight gain as humane endpoint criterion.
    vi. In table 1, please address the following:
        1. For 4TA, host should be changed to Balb/c from C57 as this tumor line is a Balb/c line. This change would result in 160 C57 and 80 Balb/c.
        2. For SUM149 fat pad studies, it is not clear why number requested is 20/study if take rate is 50%. Shouldn't this be 40/study? This change would result in 160 Nude mice.
f. In Form A, item 10a, add [redacted] for location of [redacted] euthanasia chamber.
g. In Form A, item 13a, please justify specifically why tumor resection is required.
h. In Form A, item 14, please address the following:
    i. Personnel must update ACC Regulatory Training by updating online course.
    ii. Please clarify who will conduct resection surgery and expertise with this procedure. If personnel do not have expertise, please

clarify who with expertise will train them or indicate that veterinary staff will be contacted for training.

i. In Form B, item 6c, surgery #1, please clarify that tumor bearing mice are mammary-fat pad tumor bearing mice.
j. In Form B, item 9, please address the following:
    i. For SC flank and MFP, add add "minus tumor mass" to 20% weight loss criterion and add 15% weight gain.
    ii. Remove reference to 25% increase in girth.

19-124

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2b, emergency number must be non-UIC work number.
b. In Form A, item 3, please provide the grant number assigned by NIH.
c. In Form A, item 5b, also check other and list TBD.
d. In Form A, item 5c, line 2, please add or TBD for both room and building
e. In Form A, item 6d3, the references to "mentioned in 3a-1 and mentioned in 3a 2,3) are not clear as to what these refer to. Please clarify.
f. In Form A, item 7a, include IBC # 19-049.
g. In Form A, item 8e, please address the following:
    i. Remove the reference to cost as a justification.
    ii. Remove references to Jax lab as they do not have germ free mice.
h. In Form A, item 8g, please address the following:
    i. Under fecal matter transfer, please clarify that mice will be transferred to biohazard room prior to the start of gavaging on day 1 and not on day 8 and for [redacted] add or TBD.
    ii. Under tissue harvest, please add the secondary method of euthanasia. Is a pneumothorax conducted as a secondary method?
i. In Form A, item 8h, include in this section of the protocol why only males are used for this study.
j. In Form A, item 10b, please clarify the correct secondary method to ensure euthanasia that is used with CO2.
k. In Form A, item 14, please address the following:
    i. Personnel must update ACC Regulatory Training by updating online course.
l. In Form B, item 3, also add fecal matter under oral gavage.
m. In Form B, item 7, as the pathogens in these samples are unknown, mice should be monitored at least once daily and euthanized if any of the following symptoms are noted: 20% weight loss, diarrhea, or severe lethargy. Based on current text this suggests animals will be weighed daily. Please verify this is correct and if not, please indicate the frequency of weighing, clarify that mice will be monitored daily and include the specific humane endpoints listed above.
n. Hazard form is required.

19-110

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. Test results for murine pathogens must be provided to ACC and approved by veterinary staff prior to use.
b. In Form A, item 3, please provide the institutional proposal number 00021338.
c. In Form A, item 4, please address the following;
    i. The animal numbers for LysMCre and ATX transgenic do not match with what is currently indicated in A8g. Please reconcile.
    ii. See comments below related to numbers and reconcile here for any changes.
d. In Form A, item 5c, please address the following:
    i. Correct location of housing to 172
    ii. Please indicate that animals will be housed in [redacted] post IVIS/MRI imaging.
e. In Form A, item 7b, please address the following:
    i. Complete ACC biologic form.
    ii. Include matrigel on the biologic form.
    iii. Please clarify source of LLC–CSF1-KO. Was this line created at UIC be transfection of the parent line to knockout CSF1? If not, where was this line obtained from.
    iv. Provide copies of testing for murine pathogens.
f. In Form A, item 8c, please provide a brief summary of animal experiments conducted during the last three years. If the work with animals was not initiated, please indicate that in this section.
g. In Form A, item 8e, please address the following:
    i. Under C57, please address the following:
        1. Correct "mose midely" to "most widely".
        2. According to veterinary staff, all of the lines you listed are C57; therefore, correct remove "many of our" and replace with "All of our".
    ii. For the ATX transgenic mice, it is indicated that these mice will be use as BM donors in the BM transplant experiments. However, in A8g, they are used in gain of function studies and there is no bone marrow transfer studies proposed in this protocol. Please reconcile.
    iii. For CSF1R-Cre ERT, remove the reference to the old protocol.
    iv. Please clarify the cross that will done using CSF1R-Cre-ERT and Zbtb46-cre in this section.
h. In Form A, item 8g, please address the following:
    i. Under 'orthotropic model of lung cancer' under humane endpoint for surgery complication, please remove the reference to sustained fever.

ii. The monitoring frequency mention here is same as that included in #16.
iii. Please indicate the tissue that will be harvested post mortem for histological analysis.
iv. Please clarify that why the same animals cannot be used for both IVIS and MRI imaging as both procedures are not invasive. If the same animals can be used for both type imaging, then change the animal numbers requested accordingly in here, A4, A8h, and Breeding form.
v. Correct the tables to read "# of mice for bioluminescent or # of mice for MRI". As currently listed, this suggests 10 IVIS or MRI sessions.
vi. For expts 2-4, there is no rationale as to why groups without tumors are included in a tumor study. If a few mice are required to establish a background for IVIS, this should be done as a pilot and these groups removed.
vii. Reconcile numbers in A4 and breeding form based on changes.

i. In Form A, item 8h, please address the following:
    i. Both males and females are proposed. Please clarify if these will be used in equal numbers to control for any sex differences or clarify specifically if no sex differences are expected and why.
    ii. Reconcile all animal numbers here.
j. In Form A, item 10a, please change the room number to 158 for CO_2.
k. In Form A, item 13b, there are alternatives; therefore, both of these should be answered yes.
l. In Form A, item 13c, please indicate "See A13a" as there are alternatives not being used that PI justified in A13a.
m. In Form A, item 14, please address the following:
    i. Personnel #1, please address the following:
        i. Please correct training dates to 12/10/18 for both courses.
        ii. Under training and expertise, please remove reference to CLP and SC pump as these are not part of this protocol and clarify specific expertise with intrathoracic surgery and tail vein injections.
    ii. Personnel #2, please address the following:
        i. Under training and expertise, please remove information provided and clarify expertise and training specific to the procedures on this protocol.
    iii. Personnel #3, please address the following:
        i. Please correct training dates to 8/22/17 for both courses.
        ii. Under training and expertise, please remove information provided and clarify expertise and training specific to the procedures on this protocol.
    iv. Please indicate who will oversee the animal colonies.
n. In Form B, item 4, please address the following:
    i. Line d, remove SR, as the dose proposed is for standard buprenorphine and define IT as intratracheal.

ii. Please add a line for buprenorphine SR LAB, dose of 1.0 mg/kg SC for intrathoracic surgery.

o. In Form B, item 5a, please address the following:
   i. Please uncheck the box for 'Non survival' surgery.
   ii. Please check the box for Multiple Survival as some mice will have surgery for both intratracheal injections for clodronated liposomes followed by intrathoracic delivery of LLC cells, justify both surgeries and clarify why they must be conducted at different times.

p. In Form B, item 6c, under Surgery#2, change the dose of buprenorphine SR LAB to 1.0 mg/kg.

q. In Form B, item 6d, please indicate the method of sterilization for instruments used for more than one animal in a single setting.

r. In Form B, item 6e #4- Post operative monitoring: indicate weight loss as more than 20% (minus the tumor mass) compared to control animals as the humane endpoint criterion.

s. In Breeding form, please address the following:
   i. Please reconcile the nomenclature for CSF1R mice to what is indicated elsewhere in the Form A to maintain consistency.
   ii. For ATX transgenic mice reconcile the animals numbers requested for the experiments.
   iii. If numbers change, reconcile with all other sections of the protocol.

19-120

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. Provide a copy of the CCTS grant for congruence match to the protocol.
b. In Form A, item 4, see comments below and reconcile numbers.
c. In Form A, item 7a, please address the following:
   i. Check yes for radioactivity, for RPN # indicate conducted under ACC 18-120 core protocol, and list F18.
   ii. Check yes for carcinogens, and list Estradiol (for use of E2 in drinking water).
d. In Form A, item 7d2, please address the following:
   i. Please define ShERPA, SERD, and BET here, as this is first use.
   ii. BET1 and BET2 are listed here, but there are no studies proposed in A8g using these. Please reconcile.
   iii. BRD1 (GSK 525762A) and BRD2 (XRC081) need to be listed in this table.
   iv. Describe E2 preparation for drinking water.
   v. Change "umbrella" to "core" for protocol 18-120.
e. In Form A, item 8g, please address the following:

i. In the last paragraph, prior to project 1 description, please correct the location of ketamine/xylazine administration to IP and remove reference to "into the ventral hind limb".
ii. In project #1, please address the following:
    1. Please clarify what the vehicle control group is in terms of route and vehicle administered as there are three routes of administration: oral gavage with a vehicle of (90% 10g/L CMC/10% 995 ML/L PEG 400/5ml/L Tween 80 in H2O), silastic capsule SC, and SC injection (peanut oil).
    2. The text is unclear and incomplete.
        a. The duration of dosing is not clear.
        b. The route and dose of SERD1 and 2 are not indicated.
        c. The treatments are not complete as the description does not include SERDs or the vehicles for endocrine resistant lines and for parent lines, all 7 treatments are listed in table, but only 3 are listed in the text. Please reconcile text and table.
iii. In project #2, please address the following:
    1. Under phase 1 and II,
        a. YL080 is mentioned in the title, but is not listed in A7d2, nor in the tables for project II. Please reconcile.
        b. In title, please change G1T48 to G1T38. Also, please clarify if this is a SERD as suggested in the title or a CDK4/6 inhibitor as indicated in the text.
        c. Phase 1, groups 1, 2, 3, 4, and are repeated in Phase II. Why can't groups 6 and 7 bc addcd to thc second table as this would reduce numbers by 100 mice?
        d. Dose of TTC-352 in table and used in combination does not match text which states 5mg/kg/day and used alone. Please reconcile.
        e. Text states G1T38 will be used alone, but only combination is proposed. Please reconcile.
        f. Remove specific funding from this section.
iv. In project #4, please address the following:
    1. Under phase I, please clarify that weight loss is minus tumor mass and reconcile with B9 which states 15%.
    2. Reconcile frequency of imaging with B9 which states weekly and then 3 times weekly.
    3. Under Phase II, please address the following:
        i. Please correct anesthesia to ketamine/xylazine IP.
        ii. Please clarify the reference to isoflurane if necessary. Generally, if initial dose of anesthesia is not sufficient, a supplemental dose of ¼ to 1/3 original dose should be administered.

iii. Please review the description of needle insertion as sterum and intracostal spaces are perpendicular to each other; therefore, it is not clear how can needle be inserted between.
iv. Please clarify specifically where in the heart injection is made, how correct location for needle insertion will be ensured prior to injection, and the disposition of animals in which needle is not inserted into the correct location.
v. As this is done in nude mice, please clarify the reference to moisten of hair.

f. In Form A, item 8h, please address the following:
   i. For all power analysis calculations, please clarify that the parameter being assessed is tumor volume/size.
   ii. Project 1, according to A8g 3 mice are euthanized at 1 time point and 7 mice at another; therefore the justification for N=10 is not clear as the group sizes for this study are N=3 and N=7 for the two time points. Please correct justification.
   iii. Project 2, see comment above and reconcile with A8g.
g. In Form A, item 13b, the search terms listed yield 1575 references; therefore, how did PI determine that only 73 were relevant? Please focus search.
h. In Form A, item 14, please address the following:
   i. Under specific procedures, remove CO2 inhalation euthanasia, and injection of tumor fragments as these are not part of this protocol.
   ii. For personnel #1, please correct training dates to 4/6/17 and 9/3/14, respectively.
   iii. Please clarify who will conduct IVIS imaging.
   iv. Please clarify who will conduct IC tumor cell injections and their specific expertise with this procedure. If no one has expertise, then indicate that veterinary staff will be contacted for training.
i. In Form B, item 3, please address the following:
   i. Please verify luciferin injection is SC as this is generally done IP.
   ii. Please add IC injection here.
j. In Form B, item 9, please address the following:
   i. For solid tumors, please remove last sentence as this is not a solid tumor issue.
   ii. For solid tumors, reconcile weight loss with A8g.
   iii. For spontaneous metastatic study, please clarify that in addition to solid tumor endpoints, the experimental metastatic endpoints will apply. Also, please clarify that animals will be monitored by bioimaging three times per week and monitored every day once metastasis is detected. As written, it appears imaging is done daily.
k. Hazard form is required for use of E2 in drinking water.

19-121

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, please list the background strain of all mice listed here.
b. In Form A, item 5c, please list ear wounding and indicate location.
c. In Form A, item 8e, remove "personnel name" from the list of strains.
d. In Form A, item 8g, please address the following:
    i. Under Retinal studies, remove "hypoxia" from the title as only hyperoxia studies are proposed.
    ii. Under hypertension study, please clarify the method of blood pressure assessment. Is this via tail cuff?
    iii. See comment below regarding monitoring for HLI and correct here.
e. In Form A, item 8h, please address the following:
    i. Both males and females are proposed. Please clarify if these will be used in equal numbers to control for any sex differences or clarify specifically if no sex differences are expected and why.
    ii. The Fisher's exact test does not appear to be the appropriate statistical test for determination of power and sample size for the type of data being analyzed. ANOVA followed by an appropriate post-hoc test would be the correct statistical analysis. Please reconcile.
f. In Form A, item 14, please address the following:
    i. Personnel must update ACC Regulatory Training by updating online course.
    ii. NOTE: All personnel conducting decapitation without anesthesia in mice >7 days PN must demonstration proficiency to veterinary staff.
g. In Form B, item 9, please address the following:
    i. Per ACC Guidelines, mice need to be monitored twice daily for the first 3 days. NOTE: if background is Balb/c then criteria for immunocompromised mice must be followed as this strain is highly susceptible to complications.

7. Review from Subcommittee #2

19-085

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications prior to rereveiw by the full committee and to defer the protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2a and 2b, please provide phone numbers to PI's lab not the neurosurgery office.
b. In Form A, item 4, numbers need to be reconciled between sections.
c. In Form A, item 5c, please clarify if decapitation is the correct secondary method of euthanasia, as cervical dislocation is marked in A10b. Reconcile these two sections of the protocol.
d. In Form A, item 7d2, under human cell lines, please describe the correct source of the cells. UIC is not a correct source, as these cells came from John Hopkins, the passage method (referring to standard operating procedures for passaging… is not sufficient information and provide a copy of the SOP as how these cells are maintained .
e. In Form A, item 8a, please rewrite the goal of the purposed research in few sentences. The majority of the information provided here, belongs in A8b.
f. In Form A, item 8b, please provide some background information on the cell line and tumor kinetics and tumor take rate for this line for the specific location of administration proposed under this protocol. Based on what is known about the tumor line, please indicate how quickly and to what size tumors are expected to grow within the two-week initial period.
g. In Form A, item 8g, please address the following:
    i. Please remove the first two paragraphs and start with study design tables.
    ii. The study endpoint is the point at which the desired/necessary data can be collected. Ideally, this should be prior to the humane endpoint whenever possible.
    iii. Under experiment # 1, please address the following concerns:
        1. Please clarify whether or not all animals undergo orthotopic xenograft tumor model.
        2. Please define "DMEM".
        3. Under "Surgery" #1" as buprenorphine SR LAB formulation is being used, only a single dose is administered and this dose is administered pre-operatively not post operatively. Please reconcile here.
        4. Under Non-surgical procedures: the only one listed is doxorubicin magnetic nanoparticle delivery. Please clarify what will happen to the other five groups.
        5. The time line for ALL procedures for EACH group has to be clearly stated. There is no justification at this point for survival until humane endpoints are reached. PI should be able to define scientific endpoints not are prior to humane endpoints.
        6. Please clarify which animals will be imaged via IVIS and clarify the number of images that would be needed to show a tumor is progressing, prior to determining that a specific treatment is not effective.
        7. Please clarify what is meant by incubation period. This appears to be two weeks post-tumor inoculation and should be revised.
        8. Per Experiment 1, 5 animals per group will be sacrificed at day 15 – which is assumed to be day 15 following tumor implant. However, Doxorubicin particles are delivered after

a two-week incubation period. Does this mean the animals are sacrificed the day after dox particles are delivered? How and when are imaging and behavioral tests administered?

9. Please provide description or timeline for the nanoparticle control group, intrathecal group, and intravenous group.

iv. Under experiment # 2, please address the following concerns:
   1. Please provide study design table.
   2. Please clarify if same animals from exp # 1 will be used for this experiment.
   3. Please clarify why the procedures listed under experiment # 2 could not be part of experiment # 1. Why couldn't body weight and WBC counts, etc. be measured in animals after mnp-dox treatment?
   4. The total number of animals requested is 90 in A4 and 75 here. Please reconcile.

v. Please remove the procedure for bone marrow aspiration procedure that happens post mortem.

vi. Under Neurobehavioral testing, please clarify the staging process and what happens to the data and how is used.

h. In Form A, item 8h, please address the following:
   i. Please clarify if experiment # 2 needs different group of animals and if so please reconcile.
   ii. Please clarify group size as N=5 not N=10.

i. In Form A, item 10a, please see comment above and mark the correct method that will be used.

j. In Form A, item 13a, please justify spinal cord tumor model.

k. In Form A, item 13b, search alternative to spinal tumor model.

l. In Form A, item 14, please address the following:
   i. Please correct the training dates personnel # 1: both training dates should be changed to 7/3/2018.
   ii. Please correct the training dates for personnel #: both training dates should be changed to 11/9/18

m. In Form A, item 15, please provide the signature at the correct place.

n. In Form B, item 6c, Buprenorphine SR LAB should be administered pre-operatively not post-operatively. Please correct.

o. In Form B, item 7, please describe the pain monitoring procedure, not the nanoparticle delivery procedure.

p. In Form B, item 9, please clarify the frequency of BBB assessments. According to A8g this is daily, but this section suggests only days 1 and 2 postoperative and at study endpoint. A8g frequency should be used.

19-122

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2b, change role on protocol to "1" for 1st and 3rd person listed.
b. In Form A, item 4, please address the following:
    1. According to A8g, 24/sex are required for each group, which is 48 animals/sex; therefore, please change total to 96 and clarify sex is M and F
    2. Please clarify if 6 additional animals are required per sex for non irradiated control or 6 total and what sex these animals will be. See comments under A8h.
    3. As weight is a key factor in irradiation dosing, please specify specific weight range, as well as, age range for both female and male rabbits.
c. In Form A, item 5c1, please correct room numbers to B53A and 202.
d. In Form A, item 8a, please remove the first paragraph.
e. In Form B, item 8b, please provide the rationale for testing both males and females in this specific study, as past studies have used only males.
f. In Form A, item 8g, please address the following concerns:
    i. Under objectives, please address the following:
        1. 2nd paragraph, please change "requestor" to "requested".
        2. 3rd, please clarify if use of females was also requested by sponsor and that 8 Gy is the same dose that will be used in males.
        3. 4th paragraph, please change the age rage to 16-20 to match A4, and verify that females and males will be in the same weight range.
    ii. Under Acclimation, please change last sentence to read "Any animal displaying signs of labored breeding or hyperactivity during this procedure…back in cage."
    iii. Under Pretest Measurements, please address the following:
        1. Please clarify the route of blood collection if animals have completed acclimation.
        2. Please clarify the maximum frequency of collection, as text reads "at least once.".
    iv. Under experimental design, please address the following:
        1. Specifically state the vehicle to be used.
        2. Specifically state that Neupogen, pharmaceutical grade from Amgen, will be purchased through UIC Pharmacy.
        3. As there are 24 animals per sex/group, 6 cohorts of 16 animals would be required and not 3. Please reconcile.
        4. Please include the 6 (or 12) non irradiated controls in this section and clarify if they will receive vehicle or compound and what the purpose of these animals is for this study.
    v. Under Irradiation, please clarify specifically what the Phantom is for this study.
    vi. Under Supportive care, antibiotics, please clarify the specific parameters that be used to adjust or stop antibiotic treatment.
    vii. Under Measurements, body temperature, starting with sentence 3 the remainder of the paragraph should read: "When an animals has a body temperature of below 100 F or over 104 F, body

temperature assessments and monitoring assessments will be every 2-4 hours and continued overnight. The expected critical period is days 7-10.

viii. For Clinical sign, clinical assessment, please provide a copy of Clinical assessment Form.

ix. Under blood collection: the total amount of blood collected should be 3.55/time point not 7.65, please correct accordingly.

x. Under absolute, please clarify if any of these signs are seen that animals will be euthanized.

g. In Form A, item 8h, please address the following:
   i. In paragraph #1, please address the following:
      1. Please indicate that 24/group/sex will be used and that 6 cohorts of 8/group will be conducted for a total of 48 animals/sex.
      2. Please clarify if 6 additional animals are required per sex for non irradiated control or 6 total and what sex these animals will be.
      3. Please correct total.
   ii. Under point #1, rewrite this section as there are N=24/group and not N=8/group.
   iii. Under point #3, as there will need to be 6 cohorts, please clarify the number of nonirradiated animals needed for the study and please clarify the treatment of nonirradiated animals. Are they administered vehicle or compound?
   iv. Remove point #4 as this can be addressed if needed.

h. In Form A, item 13c, please address pig as an alternative animal model.

i. In Form A, item 15, PI's signature on assurance page is required.

j. In Form B, item 4b, change the dose of ketamine/xylazine to 45/5 mg/kg.

k. In Form B, item 10, please address the following:
   i. Please move the answer to item 9.
   ii. In paragraph 1, please add that body temperature assessments will also be initiated every 2-4 hours.
   iii. Please add the following to 3rd paragraph last sentence prior to bullet points, "and will be euthanized."

8. Review from Subcommittee #3

19-109

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below and provide a point by point response to each clarifictiaon. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 5c, please identify the room numbers and buildings for each procedure conducted in this protocol (i.e. indicate where DMBA will be administered, where animals euthanatized, etc.).

b. In Form A, item 7d2, please clarify whether 100% or a lower percentage of ethanol will be used to dissolve the DMBA
c. In Form A, item 8g, please address the following:
    i. Please explain whether male and female animals will be used interchangeably or used in equal proportions and provide a rationale as to why there are either interchangeable or used in equal numbers.
    ii. Provide one or more literature references for the well characterized DMBA model that will be used.
    iii. Describe the specific site of application of DMBA on the oral mucosa and precisely how this will be done (i.e., swab, pipette, etc._.
    iv. Indicate for how long the twice weekly DMBA applications will be continued. Will this continue once tumors have developed?
    v. Describe precisely how the mice will be restrained for DMBA treatment.
    vi. Describe (based on past experience) the anticipated size of the induced tumors after 4 months and 6 weeks later in wild-type animals.
    vii. Please clarify if tumors at other sites (e.g., esophagus, stomach) are expected. If so, please indicate specifically if complications from tumors in other organ systems are expected.
    viii. Add the following two humane endpoint criteria to the list of humane endpoints: inability to eat and body score of less than 2.
    ix. Please indicate the frequency of weighing and indicate that animals will be monitored every 2 days.
d. In Form A, item 8h, consider adding tumor incidence as study endpoint along with tumor latency and size.
e. In Form A, item 9, please indicate what needs to be done with animals that are found dead (i.e., discard, save/freeze, or save/refrigerate).
f. In Form A, item 13a, please list tumor development as potentially painful condition and justify it.
g. In Form A, item 13b, please add a search for alternatives of mouse models of oral cancer; there are serveral reviews on this (e.g., Vet. J. 2016;210:7-16; Oral Oncol. 2017;73:16-20)
h. In Form A, item 14, please address the following:
    i. For personnel #1, please correct training dates to 5/18/18 for both courses.
    ii. For personnel #2, please correct training dates to 5/21/1/ for both courses.
i. In Form A, item 15, please provide the PI's signature.
j. In Form B, item 3, please indicate the site of topical DMBA administration.
k. In Form B, item 9, please address the following:
    i. Add the following two humane endpoint criteria to the list of humane endpoints: inability to eat and body score of less than 2.
    ii. Please indicate the frequency of weighing.

19-113

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, items 4 and 8.g., please explain whether male and female animals will be used interchangeably or used in equal proportions and provide a rationale for what will be done.
b. In Form A, item 8a, please indicate that dextromethorphan is a cough suppressant.
c. In Form A, item 8c, please indicate how many animals have already been used in the proposed studies during the previous three years and subtract these from the total numbers of animals requested in items A4, A8g, and A8h
d. In Form A, item 8., please address the following:
    i. Under protocol #1, please address the following:
        1. 3rd paragraph, delete last sentence on carcass disposal.
        2. 4th paragraph, delete all information after the first sentence.
    ii. Under protocol #2, please address the following:
        1. 1st paragraph, please describe the parameters that will be analyzed to assess vagal reflex.
        2. 4th paragraph, delete last sentence on carcass disposal.
        3. In Table 2, concentration of treatment is listed, but what is indicated is a dose. Please clarify if the dose is per rat or ug/kg and indicate the maximum volume to be administered.
    iii. Under protocol #3, please address the following:
        1. 1st paragraph, please describe the parameters that will be analyzed to assess vagal reflex.
        2. 4th paragraph, delete the last two sentences and details about fixation in the third sentence from the bottom.
e. In Form A, item 8h, please address the following:
    i. Please explain whether male and female animals will be used interchangeably or used in equal proportions and provide a rationale as to why there are either interchangeable or used in equal numbers.
    ii. Prior to providing details about the three protocols, please provide an explanation indicating that 2 extra rats are requested per group and provide the rationale for these extra animals. In addition, please provide an explanation as to why two extra rats per group of 6 rats (for a total of 8) are requested for protocol 1 and only two extra rats for each group of 18 rats (for a total of 20) for protocols 2 and 3.
    iii. Under protocol 1, please address the following:
        1. 3rd paragraph, delete all information after the first sentence.
        2. Explain why extra rats are needed to learn electrophysiological methods that are standard in the PI's laboratory and if they are needed, consider requesting some separate animals for this purpose. It would seem more appropriate that additional animals might be needed to address variability in response of the nodose ganglion to

drugs and/or technical problems associated with electrophysiological studies.

iv. Delete Tables 1 and 2, which are identical to those included in A8g.

f. In Form A, item 9, please indicate whether dead animals should be discarded or saved; to do both is impossible.
g. In Form A, item 13a, please address the following:
    i. Do not repeat all of A8g in this section, list the potential painful/distressful procedures to be conducted and justify why it is required.
    ii. Delete the mention of IV anesthetic administration in the listed surgical procedures as A8g indicates anesthesia will be administered IP
h. In Form A, item 13c, please replace "convenient" with "appropriate".
i. In Form A, item 14, correct training date for regulatory training to 5/22/18.
j. In Form B, item 6., please add that supplemental doses of ketamine/xylazine will be given for this 90 minute long procedure and indicate that supplemental doses will be ¼ to 1/3 the original dose.
k. In Form B, item 6c, under surgeries 2 and 3 please delete mention of anesthetic administration via venous catheter as anesthesia will be administered via IP route. In addition, reconcile the method of euthanasia in surgery 2 with the information A10a.

19-117

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, please add institutional # 00028630 to PAF information.
b. In Form A, items 5c and 10a, please address the following:
    i. Please reconcile the location of euthanasia between sections.
c. In Form A, items 8c and 8h, please describe which experiments have been conducted already in 8c and reconcile numbers in A8h for completed studies.
d. In Form A, item 8d, please insert the word "alternative" between "no" and "relevant" in the second sentence and rephrase the last sentence to more clearly indicate that intact animals consuming alcohol is necessary for the proposed studies.
e. In Form A, item 8e, please delete the last (second) sentence of the first paragraph.
f. In Form A, item 8g, please provide the following clarifications/changes:
    i. For each study, please clarify the location of euthanasia. If animals are transported from [redacted] to the laboratory for euthanasia, please describe the process for transport and clarify whether moving the animals from [redacted] prior to euthanasia will affect the postmortem study endpoints of interest.
    ii. Under Ethanol treatment regimen in rats, indicate at the end of the paragraph, indicate the method of blood collection and whether

blood is collected post-mortem or prior to euthanasia. If collected prior to euthanasia, please include volume collected and anesthesia (dose, route) used.

iii. Under injection of drugs, the volume of the SAHA and DMSO injections.

iv. Under downregulation of gene products, please address the following:

1. In the first sentence, please add "lentiviral shRNA vector" to first sentence.
2. Remove the sentence "These cannulas are .... cannot be autoclaved "and explain why sterilization of plastic material may be necessary as the cannula comes as a sterile system or delete the sentences referencing this. NOTE: if a cannula is contaminated prior to use, it should be discarded.
3. On the third page, first paragraph, insert the words "or illness" between "signs of infection" and we will contact".

g. In Form A, item 8h, please provide the following clarifications/changes:

i. Delete the sentence "if actual effects sizes are larger, then fewer rats will be used" because the actual effect sizes can only be assessed after the experiments have been completed.

ii. Describe the effects (primary endpoints) of each power calculation for each specific aim.

h. In Form A, item 13b, please add a search for alternatives of delivery systems of agents to the rat brain.

i. In Form B, item 6c, please indicate the diameter of the holes that will be drilled in the cranium and indicate that no analgesia will be used with reference to item 6.e2.

j. In Form B, item 6e2, please address the following:

i. Move information from 6f3 to this section, as section B6f is for nonrodent species.

ii. The committee suggests that the PI consider the possibility that the unrelieved post-surgical pain involved in this study may affect the epigenetic endpoints of interest. This could be addressed in a small pilot study.

k. In Form B, item 6c, in column #1, remove answer and indicate stereotaxic craniotomy.

9. Designated Review(s), Exemptions, and Lab Visits

a. Protocols

There were none this month.

b. Exceptions

Member 6 directed the Committee's attention to the following protocols requesting continuation of partial exemptions from the UIC Environmental Enrichment Plan this month. Following discussion that continuation of the partial exception was appropriate, a

motion to approve continuation was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

18-125- The PI of this protocol has requested a partial exemption from the UIC Environmental Enrichment Plan. More specifically, the PI has requested exemption from introduction of social housing partners (mesh or full contact) for all animals that will be tested with the hand reach task (HRT). During the introduction of new social pairs, it is common for animals to fight, leading to injury and the possibility of a major injury to a hand/arm/digit that would severely impair behavioral analysis of fine motor skills (i.e. HRT), a primary measure of experimental treatments.

18-127– The PI of this protocol has requested a partial exemption from the UIC Environmental Enrichment Plan. More specifically, the PI has requested exemption from social housing in the following three scenarios:1) Animals will be temporarily exempt from social housing (contact and mesh) during MPTP treatment. Individual animals may respond differently to MPTP resulting in differing levels of neurological impairment that may put them at risk for injury in a social housing paradigm. In order to prevent such injury, animals have always been housed individually during MPTP administration until stable PD is established; 2) Animals will be temporarily exempt from social housing (contact and mesh) during SPECT radioactive isolation; housing. They will be kept separate during the decay period (10 half-lives) so that urine in the excrement pans can be monitored via Geiger counter for any radioactivity present prior to removal from isolation and to prevent contamination of other animals; 3) Finally, once an animal has been selected to participate in a study involving functional assessment by hand reach task (HRT), these animals will be permanently exempt from social housing (contact and mesh) beginning with baseline behavioral HRT data collection. An injury to the arm, hand, or fingers can severely affect the HRT results. It should be noted that in all three scenarios that animals will always be housed in a room with other animals and will have visual, olfactory, and vocal contact with other animals.

c. Lab Visits

Member 6 informed the Committee that the following labs were visited as part of the post-approval monitoring program.

The following labs/investigators were visited during the last month:

Lab	ACC
[redacted] 041 [redacted]	18-177, 18-218, 19-055 17-146, 18-031 18-133 17-230 17-083, 18-219 18-200 18-076, 18-036, 28-235, 19- 17-067, 18-129

10. New Business

a. Modification of Protocol 17-157 (06)

The Committee reviewed the PI's request for a group of 4 animals to test a new cell line using the same procedures. The Committee discussed that the PI needed to address the following: that the PI had to provide additional information on the original cell lines tested as to the number of animals used in each group and the results from those groups thus far, clarify that this is group D, clarify whether new cells secrete factor and if not, justify why they are being tested. Following discussion, a motion that clarifications were needed with designated member review following full committee review for the modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

b. Modification of Protocol 18-166 (02)

The Committee reviewed the PI's request for addition of addition of germ-free mice (SKG C57 mice, C57 WT control, SKG Babl/c mice, and Babl/c WT control) for reconstitution with Alcaligens or with human fecal samples to assess role in RA and lupus. The Committee discussed that the PI needed to address the following: 1) provide an explanation as to how these studies are linked to the purpose of the original protocol, 2) reconcile numbers between sections, 3) clarify the rationale for repeating controls, 4) clarify supportive care, scoring, and humane endpoints for RA animals, 5) clarify SLE model signs and symptoms, scoring, and humane endpoints, 6) clarify source of fecal samples, and 7) revise literature search and clarify the reference to nephritis. Following discussion, a motion that clarifications were needed with designated member review following full committee review via a subcommittee of members 2, 6, and 10 for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Modification of Protocol 18-015 (01)

The Committee reviewed the PI's request fort the following: 1) addition of animals of approved strains, 2) addition of in vitro and in vivo studies, 3) addition of LPS prior to intravitral, and 4) addition of funding. The Committee discussed that the PI needed to address the following: reconcile numbers between sections, clarify nomenclature, justify LPS model. Following discussion, a motion that clarifications were needed with designated member review following full committee review for the modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

d. Modification of Protocol 18-205 (01)

The Committee reviewed the PI's request for addition of 30 athymic mice to test the effects of baicalein on ovarian cancer growth in vivo using SC xenograft model. The Committee discussed that the PI needed to address the following: clarify what baicalein is and relation to phytoprogestins, clarify how the in vitro action was determined to be

glucocorticoid independent, clarify that RU486 is also glucocorticoid receptor antagonist, clarify positive control is dexamethasome and why combination with RU486 is not included, and clarify anticipated results. Following discussion, a motion that clarifications were needed with designated member review following full committee review for the modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

e. Modification of Protocol 19-107 (02)

The Committee reviewed the PI's request for addition of NSG mice for testing a novel CXCR7 inhibitor alone or with EGFR inhibitor, Osimertinib in PDX model including new PDXs from Rush and addition of C57- EGFRDelE746_A750/T790M fl/WT for lung cancer studies and for testing the effect of EGFR inhibitor (osimertinib) in combination with CXCR7 inhibitor. The Committee discussed that the PI needed to address the following: that the total number for experiment should be 136 for - EGFRDelE746_A750/T790M fl/WT, that total for NSG should be corrected to 384 to remove breeding and potentially add NCG as alternative strain, that the timing needed to be clarified for IVIS, that the criteria for initiation of treatment needed to be when sufficient signal from IVIS is detectable, that humane endpoints needed to be revised to the following: respiratory distress, significant pallor, lack of purposeful movement upon stimulation, 20% weight loss from baseline, or body condition score of less than 2, that PDXs were part of the original protocol and did not need to be re-justified, that euthanasia should be corrected to the protocol and CO2 followed by cervical dislocation should be included for breeding and that breeding form needed to be corrected to remove NSGs. Following discussion, a motion that clarifications were needed with designated member review following full committee review for the modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

f. Modification of Protocol 18-172 (02)

The Committee reviewed the PI's request for the following: 1) Addition of Kras Tg/wt; Lkb1 fl/fl mice (80 for expts) and for Kras Tg/wt. Lkb wt/wt (40 for expts) mice (total 532 with breeding) for generation of lung tumor following adenoviral-Cre administration intranasally. Some mice will also be administered recombinant adenoviral vectors expressing Cas9 and sgRNA targeting Gfpt2 or empty vector or treated with PMM3 (phosphomannomutase 3) inhibitor, FR054; 2) Addition of 56 nude mice for additional SC tumor studies on human cell lines (H460 control, H460 GFPT2 KO, H2122 control, H2122 GFPT2 KO) for mice fed irradiated doxycycline diet; and 3) addition of funding under institutional # 00472217. The Committee discussed that there were no concerns and to administratively correct the total number for expt 1 and indicate diet is irradiated. Following discussion, a motion to approve this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

ANIMAL CARE COMMITTEE MEETING MINUTES
AUGUST 20, 2019

Attendees: Member 2, Member 6 Member 8, Member 9, Member 10, Member 11, Member 24, and Member 30

Absent: None

Guest: Member 39

1. **Minutes**

Minutes were sent for designated review determination.

2. **Announcements**

There were no announcements.

3. **Old Business**

a. Protocol 17-096 Update

Member 2 informed the committee that the veterinary staff had observed the procedure of transitioning from isoflurane to urethane that was approved under modification #3 for urodynamic rat study in a nonsurgical animal. They will also observe the PI when it is done in a surgical animal as there will be differences with the surgical stimulus and analgesia on board and provide feedback to the ACC.

b. Modification of Protocol 17-157 Mod 6

The Committee reviewed the PI's request for 4 additional animals to test allogenic cell line AG1329 in capsules for biocompatibility. The Committee discussed the following: that the previous results have shown that the capsules are biocompatible, but when implanted with xenograft cells expressing factor VIII, fibrosis and cell death was seen indicating non-biocompatibility and in order to test cell encapsulation biocompatibility further an allogenic cell line AG1329 will be used; that the cell line had not been previously tested in prior capsules and the formulation of the capsules used in other allogenic studies was not the same as the current capsules; and that the secretion profile of AG1329 cell line will be different from islet cells; supporting the need to test these cells. Following discussion, a motion to approve this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Modification of Protocol 18-162 Mod 3

The Committee reviewed the PI's request for additional animals. The Committee discussed the following: 1) that references to cohorts are unclear and that a table needed to be provided to clarify groups and # of animals per group that were completed, the # of animals that were boosted and the interval between boosts, 2) that vendor information should be removed, that the rationale for additional animals is not clear and that the letter of response contradicts the modification and the two must be reconciled. Following discussion, a motion to defer this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

4. [redacted] Director's Legislative and Facility Update

The Committee discussed the following: 1) that the rodent quarantine room was relocated to the basement to allow previous room to be used for a behavior study as it is a quieter location; 2) Facility HVAC systems have been performing well in the heat this season; 3) a member of the veterinary staff will be attending a gnotobiotic workshop in North Carolina in October in order to enhance the [redacted]'s knowledge base on the care and maintenance of gnotobiotic rodents; 4) [redacted] will take over cage wash support for mice and rats for class room satellite due to Rat parvo virus outbreak in BSB; and 5) that an ARG has a new college rating website.

5. OACIB

a. Modification

Member 2 updated the Committee to the following activity during the past month: there were 1 modification approved via administrative level, 23 modifications approved administratively following veterinary consult, and 10 modifications approved via designated review this month. In addition, there were 27 protocols that added personnel, 0 with personnel deletions, 0 that added new funding, and 0 in which animals were added to the holding protocol.

b. Continuations and Terminations

Member 2 directed the Committee's attention to the protocols for continuation and those terminated due to expiration or PI's request. The Committee discussed that all protocols had completed the appropriate continuation documents and a motion for designated member review for renewal the protocols was passed by the following vote: 8 in favor, 0 opposed, 0 abstention, and 0 recusals. In addition, the Committee discussed that the PI of 17-156 was retiring and that the protocol would be terminated. Following discussion, a motion to terminate the protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstention, and 0 recusals.

6. Review from Subcommittee #1

19-115

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed

to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, items 4, 8e, and A8g, this should be changed to CD1 strain if appears to be the strain used previously.
b. In Form A, item 3a, please clarify that this is a subcontracted project.
c. In Form A, item 5d, check no.
d. In Form A, item 8g, please address the following:
    i. Under #2, please address the following:
        1. Under bullet point 1,please address the following:
            a. Please provide a rationale for the doses listed or remove doses and indicate that doses will be identified in specific modifications with the rationale provided in modification.
        2. Under bullet point 3, line 6, change to "Animals found in these conditions will be sacrificed…"
        3. Under bullet point 5, please clarify what happens to the remaining mice.
        4. Please clarify if IV dosing will be done after oral gavage testing, whether this will be done only once.
    ii. Under #3, please address the following:
        1. Please clarify how the route will be determined for PK. Will both be used for a compound or will only one be used and will it depend on acute toxicity testing?
        2. Please state that animals that will be euthanized at 12 or 24 hours will not be removed from vivarium until just prior to euthanasia.
        3. Please address the following:
            a. Please clarify if cardiac puncture will be done percutaneously or via open chest.
            b. Please indicate how depth of anesthesia is assessed prior to procedure.
            c. Please clarify that following cardiac puncture, animals will be cervically dislocated.
e. In Form A, item 8h, 25% extra is too high for unrelated issues. This number needs to b reduced and numbers in table and A4 need to be reconciled for this issue.
f. In Form A, item 10a, list specific room numbers for each procedure and inhalation for the route for line 1.
g. In Form A, item 14, please address the following:
    i. Under procedures add following CO2 or under anesthesia after "following cervical dislocation" and add monitoring for signs of toxicity.
    ii. Under expertise, clarify expertise with euthanasia methods to be used and expertise with toxicity monitoring.
h. In Form B, item 7, move information to B9 and in 2nd bullet line 5-6, change to "Animals found in these conditions will be sacrificed…"

19-116

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, remove funding as this funding has expired and check "NO" for no external funding.
b. In Form A, item 5d, check no for maintaining animals outside vivarium for >12 hours.
c. In Form A, item 8g, please address the following:
    i. Under #2, please address the following:
        1. In paragraph #3, as the compounds are unknown how can there be a predicted water solubility?
        2. In paragraph 2, line 6, change to "Animals found in these conditions will be sacrificed…"
        3. Under bullet point 5, please clarify what happens to the remaining mice.
    ii. Under #3, please address the following:
        1. Please clarify why oral gavage route will be used for PK study if only IV route is being tested for toxicity and how a dose of 100 mg/kg was selected for oral gavage.
        2. Please state that animals that will be euthanized at 12 or 24 hours will not be removed from vivarium until just prior to euthanasia.
        3. Please address the following:
            a. Please clarify if cardiac puncture will be done percutaneously or via open chest.
            b. Please indicate how depth of anesthesia is assessed prior to procedure.
            c. Please clarify that following cardiac puncture, animals will be cervically dislocated.
d. In Form A, item 8h, 25% extra is too high for unrelated issues. This number needs to b reduced and numbers in table and A4 need to be reconciled for this issue.
e. In Form A, item 10a, list specific room numbers for each procedure and inhalation for the route for line 1.
f. In Form A, item 14, please address the following:
    i. Under procedures add following CO2 or under anesthesia after "following cervical dislocation" and add monitoring for signs of toxicity.
    ii. Under expertise, clarify expertise with euthanasia methods to be used and expertise with toxicity monitoring.
g. In Form B, item 7, move information to B9 and in 2nd bullet line 5-6, change to "Animals found in these conditions will be sacrificed…"

19-125

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 5c, please address the following:
    i. Line 3, remove 186c.
    ii. Add line 4, include [redacted], and surgery for osmotic pump insertion for procedure.
b. In Form A, item 6d, please address the following:
    i. Item 1, uncheck antibiotic water.
    ii. Item 2, all treatments administered in water need to be listed here. answer for the antibiotics in water that protocol staff will be providing to animals.
    iii. Item 3, remove the reference to "autoclavable rodent lab diet" and include source for AhR ligand diet, the product number for irradiated formulation, and include here that only irradiated diets from this source will be purchased.
c. In Forma A, item 6e, include all fasting details here (food and water) for the various experiments, maximum duration, and indicate that cages in which fasting is being conducted will be labeled "fasting".
d. In Form A, item 7c, check yes and uncheck no. List isoflurane here, room 118, and active charcoal scavenging.
e. In Form A, item 7d2, please address the following:
    i. Clarify if the fluoxetine is prepared as a concentrate that is then added to drinking water and if so, how is this prepared and sterilized and indicate if this is made fresh or stored.
    ii. L-012 needs to be listed here.
f. In Form A, item 8g, please address the following:
    i. Under specific Aim 1, please address the following:
        1. For the first study, please clarify the following:
            a. Clarify when 5-HT is administered in relation to TPH-1 inhibitors. Is this after the 4 days of gavage?
            b. Indicate the method of euthanasia for this study.
            c. Groups for study, are unclear as Vehicle group is mentioned, but there are no animals for vehicle group included; nor is it clear what vehicle is being used. 5-HT, LP-92054 or LX1032. Please clarify and if needed reconcile animal numbers here, at end of this section, in A4 and breeding form.
        2. For BNF/FICZ studies, please address the following:
            a. According to A7d2, FICZ stock solution will be dissolved in DMSO, diluted in 1XPBS and filter sterilized, but this section indicates that FICZ will be prepared in 1 ml of corn oil. Please reconcile. In addition, indicate the frequency and duration of FICZ treatment.

b. For SERT animals, please address the following:
    i. Please clarify the timing of 5HT administration in relation to BNF and FICZ.
    ii. Move last paragraph in this section prior to expt 2 description to the study that describes this work.
3. For Villin Cre/AhRff studies, please address the following:
    a. The groups listed do not include administration to TPH1 inhibitors. Please reconcile text and the groups listed. If additional groups and animals are needed, reconcile animal numbers here, at end of this section, in A4 and breeding form.
    b. Please clarify timing of all compounds administered (tamoxifen, TPH1 inhibitors, and 5-HT) and clarify when animals are euthanized.

ii. Under Specific Aim 2, please address the following:
1. Please clarify the number of groups and number of animals for SSRI administration of fluozetine. According to the text week 8 is done, but PI has still included this time point and animals for this time point in the # requested. Please reconcile.
2. Under mini-osmotic pump implantation, please address the following:
    a. The size pump proposed is too large. This pump is for rats and not mice. The correct pump for mice is SMP-310R.
    b. This section states IP implantation and B6c states SC implantation. Correct to SC and refer to Form B for details.
    c. Correct anesthesia to ketamine/xylazine anesthetized animals.
    d. The time points for this study are inconsistent in the protocol. Line 5 states 3, 14, or 28 days, line suggests 14, 21, and 28 days, and B6c1 indicates 3, 7, and 14 days. Reconcile these sections. In addition, the last sentence adds nothing to the protocol and should be removed.
3. Under IVIS imaging, please address the following:
    a. Line 9-15 need to be revised to the following; Following completion of intact imaging animals will be removed from IVIS imager and transferred prep space, reanesthetized with isoflurane in induction chamber and then placed on isoflurane mask. Following verification of depth of anesthesia via toe pinch, the fur will be clipped and skin prepped with surgical iodine and 70% alcohol and the abdomen opened. Then the animal will be immediately moved to IVIS and under isoflurane anesthesia, the abdomen will be imaged for 5 minutes to clearly specify the area of inflammation

for (e.g., ileum). Following completion of imaging, animals will be immediately cervically dislocated."

iii. Under Specific Aim 3, please address the following:
    1. Under experiment #1, please move the description of the administration of Crypo for this specific experiment to before the description of expt 2. Indicate the method of euthanasia used for this study.
    2. Under experiment #2, below table, revise the description to be specific for experiment #2 and indicate method of euthanasia used for this study.
    3. Under experiment 3, please address the following:
        a. The reference to withdrawal of water and food again is unclear as there is no prior description of withdrawal. Provide clear details of withdrawal including length for each part and the rationale for doing so.
        b. Indicate the cfu dose of for infection.
        c. Please clearly state that animals are euthanized at 1 day and 4 weeks post-injection and the method of euthanasia.
        d. Please clarify the monitoring and humane endpoints for this study.

iv. Under specific Aim 4, please address the following:
    1. Please label the study with FVB as expt #1 and the study with SERT mice as expt #2 and remove the reference to Segment IV as there are no segments I-III.
    2. For expt #1, please address the following:
        a. Please indicate the method of euthanasia.
        b. Please clarify how fecal matter is collected. Is this post-mortem?
        c. Please clarify how blood is collected. Is this post-mortem?
    3. For expt #2, please address the following:
        a. Please indicate here that Vancomycin and neomycin are pharmaceutical grade or list them in A7d2.
        b. Under day 7-8PM, please change "animals will be used for experiment" to "animals will be euthanized".
        c. Please indicate the method of euthanasia.
        d. Please clarify how fecal matter is collected. Is this post-mortem?
        e. Please clarify how blood is collected. Is this post-mortem?

v. Under Specific Aim 5, please address the following:
    1. Please clarify the frequency, duration and timeline for administration of listed compounds, and the method for euthanasia.
    2. Under GI transit assay remove reference to reference to 20th day after infection, as this study does not involve infection.

vi. For total numbers, reconcile for changes and address for all studies if males and females will be used in equal proportions.

g. In Form A, item 10a, please address the following:
   i. Column #1, do not list specific strains, list species.
   ii. List room numbers for euthanasia.
   iii. Add to the third line, mice, method 2, isoflurane 1.2-2%, inhalation, and [redacted] for euthanasia for IVIS study.

h. In Form A, item 10c, check cervical dislocation. Uncheck exsanguination as there is no description in the protocol of isoflurane use followed by exsanguination or reconcile with A8g and A10a.

i. In Form A, item 13a, please address the following:
   i. Remove line 4 starting with "for insertion…" until the end of this section.
   ii. Add acute laparotomy for exposure of intestines for IVIS imaging and justify it.

j. In Form A, item 14, please address the following:
   i. Please indicate who will be conducting infection studies.
   ii. Please indicate specifically who will conduct osmotic pump insertion and under trainer and expertise, list training will be obtained from [redacted] veterinary staff.
   iii. Please indicate who will conduct terminal surgery for IVIS imaging and expertise with this procedure.
   iv. Clarify the reference to electrophysiological studies as it is not clear which studies these are in A8g.
   v. For personnel #6, training dates need to be indicated in the appropriate sections for UIC online courses and relationship to UIC needs to be indicated.
   vi. For personnel #8, training dates need to be indicated.

k. In Form A, item 15, assurance page signature and date required.

l. In Form B, item 3, please address the following:
   i. Please check use of anesthetic for tail snips since mice older than 21 will also be genotyped and in B4 indicate what is used for this purpose.
   ii. Cardiac puncture is listed here, but not described in A8g. Please include the details in A8g (anesthetic used, dose, route, how depth of anesthesia is assessed prior to puncture) and whether this is done as percutaneous or open chest procedure.

m. In Form B, item 4, also list isoflurane.

n. In Form B, item 5a, also check survival.

o. In Form B, item 6a, include preparation for abdominal terminal surgery.

p. In Form B, item 6b, include anesthesia for terminal surgery.

q. In Form B, item 6c, surgery #1, see all comments above related to pump size, time points and reconcile.

r. In Form B, item 6c, surgery #2, describe the terminal surgery for IVIS study.

s. In Form B, item 6d, include method of instrument sterilization between animals.

t. In Form B, item 6e, table, change surgical classification to class 1 for osmotic pumps and check standard buprenorphine and remove all information under class IV.

u. In Form B, item 6e3, please include monitoring for surgical complications (ie bleeding, infections) and indicate that animals will be euthanized if this is seen.

Also if animals loss more than 20% body weight, please indicate that these animals will be euthanized.

v. In Form B, item 6e, acknowledgement box must be checked.
w. and not and check box for PI acknowledgment for post-operative care and monitoring,
x. In Form B, item 7, please address the following:
    i. For IVIS study, remove current text and just list the monitoring frequency and humane endpoints for animals post-pump insertion. For infection studies, please clarify that in addition to 20% weight loss that if severe diarrhea is seen that animals will be euthanized.

19-133

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. Condition of Approval: All personnel need to attend training session with veterinary staff to review process of using animals from the breeding protocol.
b. In Form D, item 4, update for all lines approved under experimental protocol and reconcile with A8e and Breeding form.
c. Modifications to the experimental protocols are needed to ensure congruence with breeding protocol. :
d. In Form A, item 8g, please address the following:
    i. Emla cream must be applied 10-15 minutes prior to tail snip. Please reconcile.
    ii. Remove "user protocols (listed above)" and insert "experimental protocols as identified in A4 or in subsequent modifications".

19-134

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, correct total experimental animals to 20 per sex for line b.
b. In Form A, item 6d1, uncheck antibiotic water, as this is specific for animal care staff and not the regimen listed in this protocol.
c. In Form A, item 6d2, answer for antibiotic administration in water.
d. In Form A, item 8g, please address the following:
    i. Under Aim 1, please address the following:
        1. In table and in text, change 7/13/19 to 7, 13, and 19. As written, this looks like a date.
        2. Under procedure, please address the following:

a. Please address the following regarding cardiac puncture:
    i. Please clarify if cardiac puncture will be done percutaneously or via open chest.
    ii. Please indicate how depth of anesthesia is assessed prior to procedure.
    iii. Please clarify that following cardiac puncture, animals will be cervically dislocated.
b. Line 5, please remove sentence starting with "in the pregnant mice…". Please indicate that day 19 fetuses will be decapitated.
c. Regarding pups, CO2 followed by cervical dislocation could also be used.

ii. Under Aim 2, please clarify why such a large dose range for thyroid hormone is indicated. There are only sufficient animals for one dose listed. If more than one dose will be tested, indicate the # of doses and reconcile animal numbers in A4, A8g, and Breeding form.

e. In Form A, item 10a, please clarify method #5 or #3 and not both.

19-131

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, see comments below related to fecal slurry and add additional animals if required.
b. In Form A, item 5c, list room [redacted] and list "housing after return from LIERI".
c. In Form A, item 6d3, see comments below and reconcile here.
d. In Form A, item 7d2, fecal slurry should be listed here and the preparation and storage should be listed here.
e. In Form A, item 8a, please delete first paragraph and expand on the second paragraph in a **layperson's language** as to the objectives.
f. In Form A, item 8f, include monitoring criteria and frequency, humane end points and method of euthanasia. If you will treat with antibiotics, please list the specific treatment here.
g. In Form A, item 8g, please address the following:
    i. Please clarify if males and females are used in equal proportion and if any sex differences are anticipated.
    ii. Under Expt 1A, please address the following:
        1. Define what normal diet is. This should be an isocaloric, low fat diet and not standard chow. PI should contact Envigo to discuss the appropriate control and include in A6d3.

2. List the experimental groups and number of animals similar to what is shown in Expt 1B.
3. It is strongly suggested that PI add additional C57 mice to obtain fecal samples from these mice, pool these samples to form a stock slurry for use in all animals for expt 1A and 1B. This would be a better control than mice receiving feces from different donors.
4. Indicate the method of euthanasia used.

ii. Under Expt 1B, please address the following:
1. Add # of animals per group for each group to the table.
2. See comments above regarding animals for fecal slurry.
3. Define LIM.
4. Clarify why wounding needs to be repeated.
5. Clarify method of euthanasia used.
6. Specify that after imaging mice will be return to [redacted]

iii. Under Expt 2A, please address the following:
1. Remove "no mouse will be restrained".
2. Please indicate whether or not these mice undergo corneal wounding. If they do, it a single wounding or 3 wounding and when is dox diet started in relation to the first wounding.
3. Please provide a table with strain, diet, and # of animals for this study.
4. Indicate the method of euthanasia for this study.

iv. Under Expt 2B, please address the following;
1. This experiments suggests that expt 2A involves wounding (line 6). If experiment 2A does not involve wounding then it is unclear why 2A and 2B are separate studies. Please clarify.
2. Please provide a table with strain, diet, and # of animals for this study.

h. In Form A, 8h, please rewrite this section and justify the animals by experiment.
i. Include mice for fecal collection and slurry.
ii. For expt #1A there are 3 groups of C57 mice needed as there is ND, HDF, and HDF given ND fecal slurry. Please clarify the number of mice needed per group and clarify if the repeat mentioned in the current text applies to the in vivo or in vitro portion of this study.
iii. For expt #1B, the reference to 8 per condition and then 4 per ND or HFD does not make sense. Please justify the number per group. There are no "conditions". Provide an appropriate power analysis.
iv. For expt #2A and #2B, there are 5 time points and it is not clear the number of groups (ie number of diets). Please appropriate justify the # of animals per group.

i. In Form A, item 9, please remove currently listed contacts as they are not part of this protocol and provide appropriate contact information.
j. In Form A, item 10a, please indicate room in [redacted] where euthanasia will occur and verify this is the only location.

k. In Form A, item 13b, literature search should be redone and updated accordingly as this search is not applicable to this protocol.
l. In Form A, item 14, for personnel #2, move feeding of diets and administration of fecal flora to procedures. Under expertise, clarify what specific expertise personnel have with gavage technique in mice. If known, then under trainer, indicate that personnel will be trained by veterinary staff for gavage.
m. In Form B, item 3, PI should include fecal transplant gastric gavage.
n. In Form B, item 5b, please address the following:
    1. Remove "in previous…investigator".
    2. In second sentence, change to " Multiple debridments are required as one debridment …".
o. In Form B, item 6e3, please indicate the specific antibiotic treatment and clarify the that if infection is not cleared in 7 days animals will be euthanized.

19-137

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, please address the following:
    i. Funding #4, correct institutional #
    ii. Funding #5, verify Institutional # for this proposal.
b. In Form A, item 4, please address the following:
    i. Lyz-Cre mice and crosses not listed here.
c. In Form A, item 5c, please address the following:
    i. Add room [redacted] and room [redacted] for housing of animals that have been taken out of facility and returned for survival procedures.
    ii. Please clarify that the aerosol challenge is only occurring in collaborator's lab in [redacted] and that this is done in fume hood.
d. In Form A, item 8f, please clarify the frequency of monitoring for these two models for humane endpoints.
e. In Form A, item 8g, please address the following:
    i. Page 27, Under Mechanisms for pulmonary surfactant, please clarify the specific parameter used, the effect size, the power, and the statistical test used to determine group size.
    ii. Page 29, please clarify the Donor:Recipient ratio, the # of cells administered, the volume administered, and the anesthesia used for RO route.
    iii. Page 35, under bone marrow, the monitoring frequency, humane endpoints for TBI need to match the guidelines. Please revise.
    iv. Page 38, isoflurane drop method should be changed to [redacted] and active scavenging with isoflurane machine.
f. In Form A, item 10a, column #2, please add the numbers from the procedure key below.
g. In Form A, item 13a, please address the following:

i. For LPS, remove references to sublethal doses of 10-50 mg/kg as this does not correspond to the doses administered and anything >15-20 mg/kg is lethal. Please clarify that at the doses administered in this protocol (1 mg/ml- 7 ml via aerosol route or 5 ug/g via IP route that these are sublethal doses.
ii. Add eosoinophilic esophagitis models here and justify.

h. In Form B, item 4, please address the following:
i. Complete doses in dose column. N/A is not appropriate.
ii. List K/X (100/5 mg/kg) here for surgery.

i. In Form B, item 5a, check survival.
j. In Form B, item 6a, describe preparation for BAL
k. In Form B, item 6b, add K/X for macrophage transfer.
l. In Form B, item 6c, surgery #2, list acute BAL surgery.
m. In Form B, item 9, monitoring frequency and humane endpoint criteria need to match guidelines. Please reconcile.

19-126

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below prior to rereview by the ACC. Following discussion, a motion that significant clarifications are needed and to defer the protocol for rereview by the full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. General Comment #1: modify IBC protocol for bacterial study.
b. General Comment #2: Discuss stent project with ACC.
c. In Form A, item 3, please address the following:
i. Funding # 1, item a, add that this is NIH flow-through.
ii. Funding #1, item e, please add Institutional #.
iii. Funding #2, please discuss with ACC.
d. In Form A, item 4, see comments below and reconcile numbers.
e. In Form A, item 7d2, please address the following:
i. Add FeCl and scrambled peptides to this list.
ii. Clarify how LPS is sterilized prior to administration.
iii. Remove BSA as it is listed twice.
f. In Form A, item 8c, as PI did conduct a pilot with CLP and infusion, this should be discussed here.
g. In Form A, item 8g, please address the following:
i. Under thrombosis, please address the following:
1. List the anesthesia used for this study.
2. Please clarify why a separate group of animals is required for bleed time and thrombosis. Bleeding time assay could be conducted first, animals rested for 1-2 weeks and then thrombosis study conducted. This would reduce the animals in one half.
ii. Under anesthesia, this should have been determined by now and this section needs to be revised or removed. In addition, remove all references to pentobarbital.
iii. Under drug administration, please address the following:

1. Please create a table, list each compound, the route of administration, dose(s) of administration, and the frequency of administration and time of administration. If this varies by study, this should be clear. The description is confusing and should be removed.
2. Provide the rationale for combining various drugs.
3. Remove reference to "See table in animal number…".

iv. Under GI bleeding, please address the following:
1. There are concerns regarding the ability to inject 3 times per day IV tail vein in C57 mice. IP route should be used for this study.
2. Please clarify what happens after 7 days. If animals are euthanized this should be stated and the method used should be indicated.

v. Under rpA, please address the following:
1. Define rpA.
2. Please fix symbol. Is this ug/ul or is this mg/ul?
3. Line 6, correct 0.09% to 0.9%.

vi. Under stent implant, please address the following:
1. The purpose of this study is not clear. Please discuss with ACC and clarify purpose.
2. Remove #10-12.
3. It is not clear if mice that undergo stent implant also undergo surgery for tether system.

vii. For CLP, bacteria?, and LPS, please review with ACC such that the order to the description or procedures is clear and the purpose and the specific goals are clear.

h. In Form A, item 8h, please address the following:

i. Both males and females are proposed, Please clarify if these will be used in equal numbers and if there are known sex differences.

ii. For Thrombosis, bleed time, please address the following:
1. Please see comments above related to using same animals and reconcile numbers.
2. Please clarify why the numbers are different between groups.
3. Please clarify what P2Y12 inhibitor is.

iii. Under continual infusion, please address the following:
1. Please remove + from table as peptide is not being administered along with a scrambled peptide.
2. There is no bleeding time with this group; therefore remove reference to this below the table.
3. The rationale for adding a mouse per group and for different numbers with scrambled peptides is not clear. Please reconcile.

iv. Under hemorrhage during inflammation table, please address the following:
1. Please clarify if this is rpA study.
2. Please provide a clear justification for each type of study as the information below the table does not match the table.

v. For stent study, see comments above and reconcile.

vi. There is no rationale for the mass production study provided and why all of these studies must be repeated. A much stronger explanation is required for this study.
vii. It is not clear whether peptide is administered for Aggregation/Adhesion studies or if this is just in vitro. Please clarify.

i. In Form A, item 13b, this search needs to be redone. Please discuss with ACC.
j. In Form A, item 14, please address the following:
    i. Personnel must update ACC Regulatory Training.
    ii. Please clarify the specific expertise of the personnel listed with CLP, LPS, jugular infusion and tether system.
    iii. Remove tail injection.
k. In Form B, item 3, please address the following:
    i. Under blood collection list tail bleeding and check yes or no for anesthesia use.
    ii. Under gavage list gavage for drug administration and check no for anesthesia use.
    iii. Under other treatment, list RO and IP (no anesthesia).
l. In Form B, item 6a-c, discuss stent study with ACC and revise accordingly.
m. In Form B, item 6a, please describe skin preparation for abdominal surgery in addition to the neck region.
n. In Form B, item 6c, surgery #4, please clarify if this surgery will be used with more than just CLP.
o. In Form B, item 9, please clarify what procedures/studies the monitoring and HEC is applicable to.
p. Breeding form, reconcile numbers with A4/A8h.

19-128

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, funding #1, remove as this is N/A to this study.
b. In Form A, item 4, please address the following:
    i. Correct numbers for C57 to match A8h and see comments for training.
    ii. Remove breeding animals for C57 animals.
    iii. Total for Dream KO for experiments should be 20 according to A8h. Please reconcile.
c. In Form A, item 5a, remove room number listed next to [redacted].
d. In Form A, item 5d, remove answer as this is not a justification as to why animals must be maintained in laboratory for up to 23 hours. Please state the rationale for why animal must be maintained in laboratory.
e. In Form A, item 7a, remove information under ESCRO and check no as there is no work proposed that requires this.

f. In Form A, item 7c, list [redacted] here for isoflurane use and active scavenging.
g. In Form A, item 7d2, see comments below related to antibatide.
h. In Form A, item 8g, please address the following:
    i. Under I/R stroke model, please address the following:
        1. In line 3, change site of surgery to site of incision.
        2. Line 4, change may need to be to will be.
        3. Regarding reduction in blood flow, this section states 80%, but Form B, item 6c, surgical section states 50%. Please reconcile.
        4. At the bottom of page 1 and top of page 2, please change to the following: "…from top of head, the incision will be sutured with {add the specific type of suture material and size used}.
        5. At top of page 2, indicate the specific type and size of suture material used to suture midline neck incision.
        6. Buprenorphine (0.1 mg/kg SC) must be administered prior to making any incisions, as isoflurane is used as the anesthesia. Please move to the beginning of the surgical description and correct the timing.
        7. Regarding euthanasia, please indicate the anesthetic used, the dose and route.
        8. In the second paragraph as written, the goals and study endpoints are not clear. It appears that some animals will be survived for 23 hours and undergo euthanasia for TTC, some will be survived for 23 hours and MRI and then euthanasia for TTC, and some will be survived for up to 14 days and with repeat MRIs and post-mortem analysis is not listed (ie TTC). In A8h for each study listed, please clarify the endpoint and post-mortem analysis.
        9. Regarding euthanasia of animals immediately post-MRI, please clarify if this will take place in PI's lab or in MRI facilities and indicate the method of euthanasia to be used.
        10. Include a paragraph here that discusses monitoring of animals that survive >23 hours and humane endpoint criteria. Monitoring must be a minimum of twice daily. Humane endpoints should include neurological symptoms (seizures, rolling, obtunded), inability to ambulate, lack of purposeful movement upon stimulation and BCS of less than 2.
    ii. Under Part 3, please address the following:
        1. For each antibody listed, please clarify the dose and volume.
        2. For ERO1 alpha, only one inhibitor is listed in A7d2 and in A8h. Please reconcile.
        3. Anfibatide is listed in A7d, but there is no discussion of administration here or in A8h. Please reconcile.
        4. Remove the last sentence.
i. In Form A, item 8h, please address the following:

i. Both males and females are proposed in this study. Please clarify if these will be used in equal numbers and if there are known sex differences.
ii. First paragraph for each type of ischemia, clarify the specific parameter being assessed and provide a power analysis to justify the group size. The information provided is incomplete.
iii. Please elaborate on the 50 animals requested for practice and optimize the injury condition as these studies have been ongoing in PI's laboratory for 6 years and A14a states that personnel are trained in these procedures.
iv. Reconcile C57 total- 900 for expts and

j. In Form A, item 10a, please address the following:
i. Line 1, column #2, remove information and list #3.
ii. Line 2, list method #1 and complete information for use of CO2 followed by cervical dislocation for retired breeders and excess pups.

k. In Form A, item 13a, for first surgery, please correct this to surgery for carotid artery cutdown is required in order to gain access to occlude middle cerebral artery.

l. In Form A, item 13c, this needs to be answered as alternatives were found.

m. In Form A, item 14, please address the following:
i. For Personnel #1, under training and expertise, please clarify if PI has been actively participating in these surgeries at UIC during the last 6 years.
ii. For Personnel #2, under training and expertise, please clarify if PI has been actively participating in these surgeries at UIC during the last 5 years and clarify what is meant by "animal surgery" for trainer.
iii. See comment above related to training.

n. In Form B, item 3, list other compounds in addition to antibodies.

o. In Form B, item 6c, surgery #1, please address the following:
i. Line 2, change site of surgery to site of incision
ii. Line 3, change may need to be to will be.
iii. Please change the description of wound closure for scalp to the following: "…from top of head, the incision will be sutured with {add the specific type of suture material and size used}.
iv. Please indicate the specific type and size of suture material used to suture midline neck incision.
v. Buprenorphine (0.1 mg/kg SC) must be administered prior to making any incisions, as isoflurane is used as the anesthesia. Please move to the beginning of the surgical description and correct the timing.
vi. Remove all information starting with "Then 23 hours …" until the end from surgery section and this is not surgery.

p. In Form B, item 6c, surgery 2, describe the method of euthanasia. After blood draw, how is death ensured?

q. In Form B, item 6b, please address the following:
i. Under hepatic I/R remove the reference to administration of buprenorphine post-operatively as this is a terminal acute surgery in which animals do not awake.

r. In Form B, item 9, this section needs to be answered for frequency of monitoring for the entire 14 days survival period and HEC should match what is listed above under A8g..
s. In Breeding form, the number of experimental animal for the various strains does not agree with A8h. Please reconcile and correct here.

19-138

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via a subcommittee of members 2, 6, and 10 for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. General Comment: PI needs to meet with ACC prior to submission of revisions to review description for monitoring frequency, humane endpoints, and disease sequalae..
b. In Form A, item 4, the numbers here need to be reconciled with A8h and Breeding form.
c. In Form A, item 5a, remove [redacted].
d. In Form A, item 5b, remove check marks for [redacted] and [redacted] chemical hazard, and [redacted] biohazard.
e. In Form A, item 5c, [redacted] must be listed here and Adenoviral administration (IT), P. aeruginosa IN study, Influenza (IT or IN) study, and euthanasia for P. aeruginosa and Influenza study studies must be listed here.
f. In Form A, item 5c, please address the following:
    i. [redacted] must be listed for housing of adenoviral animals after 7 days, and for housing of CLP animals
    ii. Line 1, change surgery to CLP surgery.
    iii. List Flexvet lung compliance and location.
    iv. List CT and location.
    v. List IVIS and location.
g. In Form A, item 6d1, it is not clear why antibiotic water is check. Please discuss with ACC.
h. In Form A, item 6d3, please indicate source of the tamoxifen irradiated diet.
i. In Form A, item 7c, please address the following:
    i. Please clarify scavenging for use of isoflurane in the laboratory. Fume hood appears to be incorrect.
    ii. Locations for CT and IVIS must be listed here for isoflurane use.
j. In Form A, item 7d2, please address the following:
    i. Adenoviral vectors must be listed here.
    ii. Gancyclovir must be listed here.
    iii. See comment in A8g regarding vehicle for ABT-263 study.
    iv. Please clarify how Elastase solution is sterilized.
    v. For ABT-263, please clarify how this is sterilized prior to administration.
    vi. For xenolight, please clarify the vehicle and how this is sterilized prior to administration.

k. In Form A, item 8a, JNK1 is listed here, but there are only mice included in the study for JNK2. Please clarify.
l. In Form A, item 8b, please expand in this section to specifically address the COPD, sepsis, inflammatory, cancer and emphysema models being studied.
m. In Form A, item 8g, please address the following:
    i. Under General Procedures #1, please address the following:
        1. First paragraph, line 2 remove (with oxygen) and remove first sentence under point #3.
        2. Third paragraph, please address the following:
            a. Line 2 remove (with oxygen)
            b. Remove first sentence under point #3.
            c. Please clarify how isoflurane is administered to mice for IN. Will an induction chamber be used and then animals manually restrained for IN administration or will mice be intubated as described under intratracheal instillation?
        3. For each route of administration of influenza and for each strain influenza, clarify the dose to be administered and the sequalae of the animals post-infection.
        4. In the second and fourth paragraph, please remove "For survival experiment", as the humane endpoints are applicable to all animals infected regardless of planned time points.
    ii. Under General Procedures #2, please address the following:
        1. Please indicate the dose of ketamine/xylazine in mg/kg.
        2. One expt in study design references inflating the lungs with PBS or agarose which is not described here. Please clarify this issue here.
    iii. Under General Procedures #3, please address the following:
        1. Write a separate paragraph for Flexivent, IVIS, and micro CT
        2. For Flexivent, please address the following:
            a. Please clarify if PI has Flexivent instrumentation and if not, where it will be obtained from.
            b. Please describe the dose anesthesia administered for this purpose in mg/kg dose and not mg/ml dose.
            c. Please refer reader to Form B for details of tracheostomy and wound closure or if animals are intubated via oral cavity then remove reference to tracheostomy.
            d. Please describe post-operative analgesics here if tracheostomy is conducted.
            e. Please clarify frequency at which this test is done and the maximum number of times this procedure will be conducted.
        3. For micro CT, please address the following:
            a. Please indicate anesthesia will be induced with 5% isoflurane and animals maintained on1.5-2 % isoflurane for this procedure.

b. Please clarify if core personnel will conduct micro CT.
c. Please clarify which animals will undergo micro CT, and clarify frequency at which this test is done and the maximum number of times this procedure will be conducted.

4. For IVIS, please address the following:
   a. Remove reference to core protocol for this procedure.
   b. Please indicate anesthesia will be induced with 5% isoflurane and animals maintained on1.5-2 % isoflurane for this procedure.
   c. Please include details here on Xenolight administration.
   d. Please clarify which animals will undergo IVIS, and clarify frequency at which this test is done and the maximum number of times this procedure will be conducted.

iv. Under General Procedures #4, please address the following:
   1. Correct dose of buprenex to 0.05 mg/kg SC for two doses.
   2. Skin must be closed with a monofilament suture. Please indicate the specific suture material to be used.

v. Under General Procedures, a section for blood collection should be added to include method, volume collected and frequency of collection.

vi. Under study details, please address the following:
   1. Define COPD the first time it is used.
   2. Clarify POZ as this is not listed in A4 or A8e.
   3. Under study #2.1, please remove details of the procedure from this section as this should be covered under general procedure #3. Please clarify the timing between Flexivent and procedure B and why if animals are euthanized right after Flexivent it is necessary to allow them to recover from anesthesia prior to reanesthetizing them for BAL and euthanasia.
   4. Under study #2.2, the procedures should be described under general procedures and not repeated here. Also reference here to laparotomy and exsangination via renal artery are unclear as the lungs and heart are isolated en bloc. Under procedures, please review and clear describe the sequence of procedures.
   5. Under study #4, define GCV.
   6. Under study #5, please address the following:
      a. Reconcile vehicle with A7d2 which includes DMF.
      b. Study #5a, please clarify how mice are euthanized prior to harvesting of the lung.
   7. Under study 7, clarify what procedures will be done as none are described.
   8. Under study #8, please address the following:

a. Under A, please just indicate administration of Ad-Cre or empty vector and dose and do not repeat details of administration.
b. Under B1, clarify frequency of "general monitoring", and when monitoring will be increased.
c. Under B2, please address the following:
    i. Change 6% to 5%.
    ii. Clarify frequency of CT.

9. Under study #9, please address the following:
    a. It is not clear how many different groups/time points there are or which strain of virus will be used.
10. Under study #10, please address the following:
    a. Time points listed here do not match with those listed under procedures.
11. Under study #11, please address the following:
    a. Please clarify how mice are euthanized prior to lung isolation.
12. Under study #12, please address the following:
    a. Please clarify how mice are euthanized prior to lung isolation.

n. In Form A, item 8h, please address the following:
    i. As there are multiple parameters being assessed, please clarify the parameter used for power calculation and the SD used to calculate the ES.
    ii. Provide rationale for repeating experiment.
    iii. Both males and females are proposed in this study. Please clarify if these will be used in equal numbers and if there are known sex differences.
    iv. For study 8 please clarify the two procedures.
    v. Provide a summary table with strain and study with # of animals.
o. In Form A, item 10a-d, table needs to be redone.
p. In Form A, item 12b, check yes and uncheck no for analgesic use.
q. In Form A, item 13a, add LPS/elastase model and justify it.
r. In Form A, item 13b, under period of years searched, please revise to indicate the specific years searched (ie. 2000-2019). In addition, PI needs to provide a more focused search for influenza studies.
s. In Form A, item 14, please address the following:
    i. UIC emails must be used.
    ii. Provide training dates must be provided.
    iii. Clarify who will conduct LPS/elastase, blood sampling, gavage, and experience with these procedures.
t. In Form A, item 15, PI must sign assurance page.
u. In Form B, item 3, please address the following:
    i. >5 mm of tail should NOT be collected. Please see UIC Guidelines and revise this section accordingly.
    ii. Please clarify the reference to anesthesia for gavage.
    iii. Include LPS, LPS/elastase, and adenovirus administration.

v. In Form B, item 4, list doses of ketamine/xyalzine used for surgery or sedation and not for euthanasia.
w. In Form B, item 5a and b, correct for scope.
x. In Form B, item 6a, this must be completed for each surgery.
y. In Form B, item 6b, this must be completed for each surgery.
z. In Form B, item 6c, this must be completed for each surgery.
aa. In Form B, item 9, please address the following..
    i. For Kras mice, clarify frequency of "general monitoring", when monitoring will be increased. Remove reference to PET.
    ii. Infectious disease studies need to be included here with monitoring and humane endpoints.
    iii. CLP needs to be included here with monitoring and humane endpoints.
    iv. LPS needs to be included here with monitoring and humane endpoints
bb. Breeding form., please reconcile with above.
cc. Hazard form, remove gancicilovir. Clarify that animals with influenza or PA will remain in BSL2 for entire project including euthanasia.

7. Review from Subcommittee #2

19-085

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review via designated review process for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 3, please address the following:
    i. Item c- correct title.
    ii. Item e, correct institutional #.
b. In Form A, item 4, see comments below and revise the number required.
c. In Form A, item 5c, please address the following:
    i. Line 4, it is not clear what AM means. Please remove and indicate housing room.
    ii. Define BBB with first use.
d. In Form A, item 8a, please add (i.e., less toxic) following superior to clarify what is meant.
e. In Form A, item 8b, discuss comment regarding time window for treatment administration with ACC.
f. In Form A, item 8c, this section suggests that PI has conducted in vivo studies with tumor cells as it refers to tumor parenchyma. Please clarify the number of rats in which cells were administered, the duration of the study, and the sequelae of the animals post-tumor administration including signs and symptoms at what time points.
g. In Form A, item 8g, please address the following:
    i. Depending on the response to A8c, a pilot study of 5 or 6 animals needs to be conducted without drug administration to determine

the growth kinetics, sequelae, monitoring frequency and humane endpoints.

ii. General Comment: animals in the toxicity arm and in the efficacy arm undergo identical treatment and there is ample biologic material to take from each animal to complete both types of testing. Therefore, all mention of separate arms should be eliminated and the research aims completed in one set of 30 animals (an N=5 in each of 6 groups).

iii. In study diagram, please address the following:
    1. Modify flowchart to depict one set of 30 animals rather than showing 2 arms.
    2. Remove all labels at the bottom of the page.
    3. List treatment in one box and not two as having two "treatment" labels makes it appear as if there could be two times for treatment.
    4. Consolidate the boxes under endpoints to reflect one group.
    5. Clarify that the treatment ends when animals reach humane endpoints.

iv. Define all abbreviations with first use, including POD.

v. In the study design text, starting with line 11, replace text with the following: 30 rats will be used and all animals will be implanted with cells on day one of the study. On day 15, they will be sorted into six treatment groups, as depicted in the flow chart and each animal will undergo baseline blood (150 microliters) blood draw prior to initiation of treatment. Beginning on day 20, IVIS imaging will be completed every 5 days and BBB score assessed. A second 150 microliter blood sample will be obtained from two animals in each group at the time of IVIS imaging. The blood will be obtained on a rational basis so that blood is taken from each individual animal only three times at most (baseline, once during study, and at sacrifice). Thus, at the time of imaging on Day 20, blood will be obtained from 2 animals per group (2x6 =12), on Day 25, blood will be obtained from 2 different animals in each group, and on day 30. Animals will be sacrificed when they reach humane endpoints. The median survival time of animals implanted with this cell line is 31 days.

vi. Under procedure, orthotopic xenograft, #1, please revise to the following: "Anesthesia will be induced by 5% isoflurane in a induction chamber and maintained with 1-3% isoflurane with a nose cone. Depth of anesthesia will be monitored via toe pinch and observation of respirations prior to surgery and every 15 minutes. All anesthesia used in protocol will be the same regimen." In addition, as the same anesthesia regimen is used repeatedly. , you can state this once and say for all procedures.

vii. Under procedure, IT DOX MNP/DOX/DMEM, #1, please revise to the following: "Following the 15-day tumor growth period, the doxorubicin loaded magnetic nanoparticles or doxorubicin alone or DMEM will be administered based on treatment groups. Rats will be anesthetized described previously."

viii. Under procedure, DOX, DMEM, #1, please revise to the following: "Following the 15-day tumor growth period, the intravenous doxorubicin or DMEM will be administered based on treatment groups. Rats will be anesthetized described previously."

ix. Under procedure measures of efficacy, please address the following:

1. Change title to "Measures of Efficacy and Toxicity.
2. Add a new #3 and from under toxicity add point regarding weighing animals.
3. Change current #3 to #4. Revise as follows: "Blood will be collected to assess: 1) hLINE-1 human DNA marker as a predictor of response to therapy. hLINE-1 is quantified in the blood via PCR and serves as a marker for tumor burden in athymic rats and 2) white blood cell number from peripheral blood samples to access systemic toxicity. 150 ul blood sample will be collected from each animal on day 15 prior to treatment as a baseline sample. In addition, beginning on day 20, a second 150 microliter blood sample will be obtained from two animals in each group at the time of IVIS imaging. The blood will be obtained on a rational basis so that blood is taken from each individual animal only three times at most (baseline, once during study, and at sacrifice). Thus, at the time of imaging on Day 20, blood will be obtained from 2 animals per group (2x6 =12), on Day 25, blood will be obtained from 2 different animals in each group. collected every five days after treatment via lateral tail vein. This blood will be collected every five days from
4. Change current #4, to #5.
5. Add a new #6, and from under toxicity add bone marrow cellularity.

x. Remove toxicity cells as this is now incorporated above.

h. In Form A, item 8h, revise to one power analysis for both efficacy and toxicity. PI has not justified and justify 25% additional animals. As tumor take rate is 100%, 25% additional animals seems high. As there are 6 groups, 1 additional per group (total 6) in case of complications is reasonable. In addition, if pilot is required add animals for pilot study.

i. In Form A, item 10 a, method is #5 not #1

j. Principal Investigator should sign on Principal investigator line.

k. In Form B, item 4change dose to 1-5%

l. In Form B, item 6f, remove response. This table is for non-rodent mammals.

m. In Form B, item 7, remove answer. Item 7, include at the bottom "See also Item #9)

n. In Form B, item 9, animals should be weighed every five days. Since the animals are expected to show signs of disease as they near the expected endpoint of 31 days, monitoring should be increased. Please discuss humane endpoints and monitoring frequency with ACC and revise accordingly. Monitoring frequency and humane endpoints in A8g should be reconciled with B9.

8. Review from Subcommittee #3

19-112

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2, please check the boxes regarding role in project and correspondence.
b. In Form A, item 3, please provide add institutional # to this section.
c. In Form A, item 4, please add grams to indicate the unit of weight.
d. In Form A, item 7c, please check the "yes" box and uncheck "no" box. List isoflurane, location, and scavenging method for use in perfusion/exsanguination procedure.
e. In Form A, item 8a, please delete "illicit drugs such as" in first sentence, as alcohol is not an illicit drug. In addition, please add a sentence that paraphrases the first sentence of A8b to provide proper context.
f. In Form A, item 8g, please address the following:
    i. In the first paragraph, please clarify why a single volume of ethanol (10 ml/kg) is listed when a dose range of 1-2 g/kg of 20% ethanol will be injected, i.e. provide the volume range that will be administered to accommodate for the varying dose of 1-2g/kg of 20% ethanol to be administered.
    ii. In the paragraph about exsanguination, please clarify how the heart will be accessed for perfusion (e.g., via thoracotomy) and how soon after the access to the heart is established the exsanguination will commence; this is unlikely to take 5-10 minutes and therefore please replace the word "exsanguination" in the last sentence with "completion of perfusion".
g. In Form A, item 8h, please address the following:
    i. Under Experimental Group b, please replace the words JQ1 with "inhibitor" as more inhibitors will be tested than just JQ1.
    ii. Please clarify why vehicle and ethanol only groups must be repeated for each inhibitor and the same groups cannot be used for all inhibitors.
    iii. In the last sentence, please replace the word "Similar" with "The same" or "Identical".
h. In Form A, item 13b, please narrow the second search by adding the various inhibitors being assessed into the search profiles.

19-132

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed

to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 1 recusal.

a. In Form A, item 5c, please identify the locations of the alcohol administration and the drug injections.
b. In Form A, item 8e, please add the words "have been shown to" between "mice" and "consume".
c. In Form A, item 8g, under part B, please add the word "euthanized" between the words "from" and "postnatal" in the first line of page 4.
d. In Form A, item 10e, please provide the requested information.
e. In Form A, item 14, please address the following:
    i. For personnel #3, please correct training date for ACC to 7/31/19.
    ii. For personnel #4, please correct training date for ACC to 8/14/19.
f. In Form B, item 6e3, please add neurological signs/symptoms as humane endpoint criterion for surgical complication.

19-129

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, items 8a. and 8b, please address the following:
    i. Move the text in A8a to A8b and the text from A8b to A8a, as the latter is more lay description.
    ii. In the original A8a, line 2, insert "being treated for depression" between mothers and increases.
    iii. In the original A8a, line 15, change the words "in vivo" to "ex vivo".
    iv. In the original A8b, line 1, insert the words "for the treatment of depression" before the words "in pregnant mothers".
b. In Form A, item 8d, please change the words "in vivo" in the last line to "ex vivo".
c. In Form A, item 8e, please delete the sentence "These mice …. Laboratory".
d. In Form A, item 8f, please delete the second sentence, as this is not relevant for monitoring and humane endpoints.
e. In Form A, item 8g, please address the following:
    i. Under Prenatal SSRI Exposure, please clarify the specific devise used and how the tube is adequately ventilated.
    ii. Under Food Restriction, describe the actual manner in which this will be done and reconcile this with the explanation in B10.
    iii. Under Behavioral Training and Testing, Behavioral Test 2, please replace the word "Proponent" with Prepotent".
    iv. Under Electrophysiology, please delete the entire paragraph about the ex vivo study details.
f. In Form A, item 8h, please address the following:

i. Please clarify that dams are treated.
ii. Please clarify that for each strain 12 female and 6 male breeders for a total of 54 breeders are requested.

g. In Form A, item 9, please the disposition of dead animals. Check one of the three first boxes.
h. In Form A, item 10a, line 1, column 3, list isoflurane (1-5%).
i. In Form A, item 10f, remove the last two sentences and add "which requires a very rapid method of euthanasia.
j. In Form A, item 13a, please address the following:
   i. Remove "and restraint in the MRI scanner" in the first line.
   ii. Remove "For restraint in the scanner…monitored."
k. In Form A, item 14, please address the following:
   i. Please verify that the only personnel conducting decapitation without prior anesthesia is Personnel #6. If not, please list under appropriate personnel. Personnel other than #6 will need to demonstrate proficiency to veterinary staff.
   ii. Personnel #1, correct training dates to 11/27/18 for both courses.
   iii. Personnel #2, under procedures, delete hippocampal dissection, as this is post-mortem. Correct dates of training to 5/12/17.
   iv. Personnel #3, please correct dates for training to 3/2/18 for both.
   v. Personnel #4, please correct dates for training to 5/29/19 and 5/30/19.
   vi. Personnel #5, remove brain slice electrophysiology as this is an ex vivo procedure and clarify what procedure personnel will conduct in vivo. Correct dates of training to 9/4/18 and 9/3/18.
   vii. Personnel #6, under procedures, delete hippocampal dissection, as this is post-mortem.
l. In Form B, item 10, please remove the last paragraph, as the restraint will be less than one hour.
m. In Form B, item 11, please change the number to 96/strain to reflect only the offspring.

9. Designated Review(s), Exemptions, and Lab Visits

10. New Business

a. Semi-Annual Inspections/Review Fall Schedule

Member 2 referred the Committee to the schedule for reviews and inspections and the Committee discussed scheduling for participation.

b. Modification of Protocol 19-089 Mod 2

The Committee reviewed the PI's request for addition of 2 animals for pilot study to test the use of laparoscopic procedure as a less invasive route to open laparotomy for administration of alpha synuclein to the gut muscle. The Committee discussed that both species were similar and that this species was appropriate for the pilot study to assess method and verify targeting and injection volume in gut wall. If pilot is successful, laparoscopic procedure will be added as an alternative to open laparotomy 2) Addition of

fine motor skills testing using hand reach task (HRT). Following discussion, a motion to approved this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Modification of Protocol 17-137 Mod 6

The Committee reviewed the PI's request for a change in PI due to reorganization of the unit. The Committee discussed that the new PI was the core director for this core protocol and well qualified as PI. Following discussion, a motion to approved this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

d. Modification of Protocol 18-200 Mod 2

The Committee reviewed the PI's request for addition of 48 ITGB4ECKO and 48 ITGB4 fl/fl mice for CLP model. The Committee discussed that the PI needed to address the following: clarify the reference to LPS, clarify study endpoint time points, justify additional animals requested, indicate location and surgeon, clarify aseptic preparation, and justify the procedure. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

e. Modification of Protocol 17-209 Mod 2 and 3

Mod #2

The Committee reviewed the PI's request for addition of RO dextran injection to visualize cerebrovasculature during 2-photon imaging and addition of personnel. The Committee discussed that the PI needed to clarify that personnel would only assist in surgical anesthesia and preparation and would not be conducting the surgery. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

Mod #3

The Committee reviewed the PI's request for addition of AAV-GFP stereotaxic injection in PPT1 and TSC1 KO mice and WTLM as an alternative to intrauterine administration, for addition of 64 PPT1 KO mice and 64 WTLM for testing the effects of NtBuHa administered in the drinking water, and for addition of personnel. The Committee discussed that the PI needed to clarify the specific site of injection and coordinates, dose and volume, and if this was same site as Cre injection during same procedure; clarify training dates, and that new personnel would only assist with procedure. Following discussion, a motion that clarifications are needed to secure approval with designated

member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

f. Modification of Protocol 18-250 Mod 3

The Committee reviewed the PI's request for the following: 1) addition of 80 mice to assess the effect of hunger or thirst following 17 hour fasting from food or water on hyperalgesia expressed during morphine withdrawal and 2) addition of personnel. The Committee discussed that the PI needed to address the following: to clarify that animals would be fasted from food or water for 17 hours, clarify cage labeling, and disposition of mice after testing, and update training date. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

g. Modification of Protocol 19-016 Mod 3

The Committee reviewed the PI's request for 5 additional rats for addition of testing medical grade air as a carrier for isoflurane anesthesia to establish guidelines for ventilator settings and that the rats would be transferred from another protocol in which they were used for a PK study. Following discussion a motion to approve this modification was passed by the following vote: 6 in favor, 0 opposed, 0 abstentions, and 2 recusals.

ANIMAL CARE COMMITTEE MEETING MINUTES
SEPTEMBER 17, 2019

Attendees: Member 2, Member 6, Member 8, Member 9, Member 10, Member 11 and Member 24

Absent: Member 30

Guest: Member 41

1. **Minutes**

Minutes were sent for designated review determination.

2. **Announcements**

Member 2 reminded the Committee of the dates for semi-annual reviews and inspection.

3. **Old Business**

a. **Satellite Facility**

The Committee discussed that the PI had worked with the veterinary staff and updated the application and SOPs for new gnotobiotic satellite, that members of the IACUC would inspect the new facility and that following some final edits the application and SOPS would be sent for designated review determination and that the PI would also submit a modification for some pilot animals to test procedures for maintenance of gnotobiotic condition.

4. [redacted] **Director's Legislative and Facility Update**

The Committee discussed the following: 1) that 3 month follow-up testing of the room in which MPV had been identified was negative for MPV, the room was released from quarantine, and that sentinels would still be tested monthly for the next 3 months; 2) that COD HVAC was be serviced and air pressure differentials balanced and the work was expected to be completed by the end of September and that the facility would be sanitized and inspected in preparation for reactivation and re-occupancy, 3) that 32 students were enrolled in GC 470, and 4) that SCAW would be hold at UIC this November and that information for registration would be provided to members.

5. **OACIB Update**

a. **Modification**

Member 2 updated the Committee to the following activity during the past month: there was 1 modification approved via administrative level, 20 modifications approved administratively following veterinary consult, and 8 modifications approved via

designated review this month. In addition, there were 38 protocols that added personnel, 0 with personnel deletions, 2 with addition of funding, and 0 addition to the holding protocol.

b. Continuations and Terminations

Member 2 directed the Committee's attention to the protocols for continuation and those terminated due to expiration or PI's request. The Committee discussed that all protocols had completed the appropriate continuation documents and a motion for designated member review for renewal the protocols was passed by the following vote: 7 in favor, 0 opposed, 0 abstention, and 0 recusals.

6. Review from Subcommittee #1

19-141

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. Please contact ACC prior to initiating protocol revisions to review numbers.
b. In Form A item 2b, please provide complete email address for the second project staff.
c. In Form A item 3, please address the following;
    i. Funding #1, please add RO1 to grant number.
    ii. Funding #2, please add F30 to grant number.
    iii. Please remove funding support 3 as this is not part of this protocol
d. In Form A item 4, CD1 mice and several transgenic lines described in A8e & g were not accounted for in this section. Please reconcile.
e. In Form A item 6c, check "yes" for single housing, uncheck 'no", and justify for time-mated studies.
f. In Form A, item 7d2, please clarify how the DMP solution is sterilized and clarify that the collagen membranes are sterile.
g. In Form A item 8b, include additional scientific background information on the role of dentin matrix proteins in osteoblast and odontoblast differentiation.
h. In Form A item 8e, please reconcile all transgenic lines listed here with A4
i. In Form A item 8g, please address the following:
    i. Under Exp1, please address the following:
        1. Line 11, please change to indicate "each will be given only once per stain at prior to euthanasia.
        2. Line 13, please change "would be" to "will be".
    ii. Under Expt 4, indicate method for euthanasia.
    iii. Under Expt 5, please address the following:
        1. Indicate the age of recipient animals for this experiment.

2. Create a table to clarify the donor animal genotype, sex, #, and date of pregnancy of donor and recipient animal genotype, sex, and # for each donor group. These numbers should match those in A8h.
3. Please clarify the # of cells recombined with dental epithelium.

iv. Under Expt 6, please address the following:
1. Indicate approximate ages of mice.

j. In Form A, item 8h, please address the following:
i. Experiment #5, please clarify time points for tooth germs as A8g has two time points. Please ensure that numbers match with A8g. See comments above.
ii. Table, please address the following:
1. Please clarify why a separate C57 group for each KO group.
2. Expt 5, see comments above and reconcile.
3. CD1- control for one is not clear as this is a control for group 16.
4. Wnt1- ping agent only is unclear. Please clarify.
5. Reconcile numbers with A4 and Breeding form.

k. In Form A, item 10, the numbers in column 3 should be listed in column 2 (method) respectively.
l. In Form A, item 14, PI needs to update online ACC Regulatory Training.
m. In Form B, item 3, tetracycline should be changed to oxytetracycline.
n. In Form B, item 6c, under surgery #1, should reconcile time points for timed pregnant mice euthanasia with A8g.
o. Breeding Form, correct to match A8g/h and reconcile with A4.

19-126

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 4, reconcile numbers. See comments below
b. In Form A, item 5c, line 4, add jugular catheter surgery here.
c. In Form A, item 7d2, please address the following:
i. Add FeCl to this list.
d. In Form A, item 8g, please address the following:
i. Under bleeding time, clarify how tail is sealed and in line 8, add "same" prior to animals.
ii. Under #2, please clarify if it is time to clotting that is being assessed.
iii. Under drug administration, add daily administration for GI study to table, indicate that isoflurane anesthesia is used for RO

administration, and under GI bleeding, please indicate that mice are euthanized after 7 days and method of fecal collection.
   iv. Under rpA, correct units.
   v. Under CLP, LPS, and E. coli, indicate the method of euthanasia used for these studies.
   vi. Under time points for infusion, indicate a single time point.

e. In Form A, item 8h, please address the following:
   i. Under thrombin, bleed time, and sepsis studies, please clarify the parameter assessed.
   ii. Under CLP, LPS, E coli continual infusion, correct number to 24.
   iii. Under change X (# injury sites) to divided by # injury sites.
   iv. Provide a justification for N=5 for two-photon study
   v. For mass production, either state the two conditions to be tested or remove this and reconcile for total numbers.
   vi. Correct number of breeders and total.

f. In Form A, item 13b, please address the following:
   i. For searches 1 and 2, please indicate yes for alternatives
   ii. For search 3, add hemorrhage to the search terms and search all years.

g. In Form A, item 13c, please indicate that there are other thrombosis models, but that these are either more or equally invasive and that studies in mice are essential for preclinical data.

h. In Form A, item 14, please address the following:
   i. Pi needs to update online ACC Regulatory Training.
   ii. Correct training dates.
   iii. Please clarify the specific expertise of the personnel listed with procedures and if training is required and that veterinary staff will train.

i. In Form B, item 6e, in item 3 under table, correct for CLP/jugular surgery.

j. Breeding form, reconcile numbers with A4/A8h.

19-147

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 2b, please remove 1 from column 2.
b. In Form A, item 4, numbers need to be reconciled with Breeding form and TD should be defined.
c. In Form A, item 5c, list housing 7 days post Ad-administration.
d. In Form A, item 7d2, please include that the Ad-Cre vector will be diluted utilizing sterilized PBS and describe how stock is stored.
e. In Form A, item 8a, line 5, change "was" to "will be".

f. In Form A, item 8d, please move "The mouse has thus…or over expressed (transgenic mouse)" to the beginning of A8e, as this justifies a specific species and not animals in general which is the question asked.
g. In Form A, item 8g/h, please address the following:
    i. Remove note as this is not required.
    ii. In second paragraph remove "by tamoxifen" as Cre will be an Ad-Cre in these studies.
    iii. Under Construct, please address the following:
        1. In 1st paragraph line 2, remove different.
        2. Clarify time points for euthanasia.
    iv. Under monitoring frequency, remove "The mice with Kras…post-Ad-Cre instillation". This is not required.
    v. Remove "Surgical Techniques: Anesthesia" and change "Euthanasia for tissue collection".
    vi. Provide appropriate justification of numbers with the adequate statistical analysis.
    vii. Please indicate if equal number of male and female mice will be used or they will be used interchangeably
h. In Form A, item 9, please check the box for other contacts under 'dead animals'.
i. In Form A, item 10a, please address the following:
    i. Line 1, column #2, remove answer and list #5 and under column #3, list ketamine/xylazine and dose.
    ii. Line 2, column #2, remove answer and list #1, under column #3, remove answer, and under column #5 add 158.
j. In Form A, item 10c, uncheck the box.
k. In Form A, item 13a, please justify why this specific model is needed.
l. In Form A, item 13b, the first search should be made more focused using precise search terms for alternatives. Correct # of references to 37 and 29 for last two searches.
m. In Form A, item 14, please remove IT under personnel #2 under procedures.
n. In Form B, item 3, replace intratracheal administration with oropharyngeal instillation.
o. In Form B, item 10, remove answer as this section is N/A.
p. Breeding form, the total number of pups that needs to be corrected and reconciled with A4.

19-153

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 2b, remove "1" from role on protocol from column #2.
b. In Form A, item 3, please address the following:
    i. Funding #1, please add 00317107 for PAF number.
    ii. Funding #2, please add 00017256 for PAF number.

c. In Form A, item 4, please address the following:
    i. Line a, please define TD here.
    ii. Add Cre to the description where appropriate to clarify strain.
d. In Form A, item 5c, please address the following:
    i. Please list housing post-CLP/LPS and post-hyperoxia.
    ii. Please add [redacted] for DTA mice and indicate tamoxifen administration and euthanasia.
e. In Form A, item 7a, update IBC number to current and add DTA mice to the last column.
f. In Form A, item 7d2, please address the following:
    i. Add bleomycin here.
g. In Form A, item 8d, please address the following:
    i. Please include why animals are important to sepsis and fibrosis studies.
    ii. Please move "The mouse has thus…or over expressed (transgenic mouse)" to the beginning of A8e, as this justifies a specific species and not animals in general which is the question asked.
h. In Form A, item 8e, define TMX.
i. In Form A, item 8f, please address the following:
    i. Please review with ACC, the mice listed here and the time frame of experiments and maintenance for monitoring frequency and humane endpoints.
    ii. Remove "during exposure", as mice that display these symptoms at any time must be euthanized.
j. In Form A, item 8g, please address the following:
    i. Clarify if males and females are used interchangeably or in equal numbers and whether any sex differences have been noted.
    ii. Indicate methods of euthanasia for the various studies and refer to B9 for monitoring and endpoints.
    iii. Experiment #1, please address the following:
        1. Please clarify that only some groups will be allowed to recover for 14 days.
        2. Please clarify that levels are monitoring and recorded daily.
        3. Under monitoring of mice, please clarify what endpoints will be used as humane endpoint criteria should mice appear sick.
        4. Following the description of the 3 groups, please clarify what happens to groups 1 and 2 after 72 hours and to groups 3 and 4 after the two week recovery.
    iv. Experiment #2, please address the following:
        1. Define AEC.
        2. Include KEAP KO description here as well.
    v. Experiment #4, please address the following:
        1. Time points are inconsistent. Please reconcile.
        2. Number of groups is 8 and not 4 as there are two doses indicated. Please reconcile.
    vi. Experiment #5, please address the following:
        1. Please correct the first sentence to indicate that some animals will be recovered for 3 or 7 days.
        2. Please correct timing for groups 3 and 4.

vii. Experiment #7, please address the following:
    1. Surgical description is incomplete. Either match B6c1 or remove details and refer to Form B
    2. There are only 4 and not 5 groups. Please reconcile.
    3. Clarify why some strains have a day 7 group.
viii. Experiment #8, separate description for low dose versus high dose study and clarify which groups will be in high dose group as this would only have one time point and not 4.
ix. Treatments, indicate the route of tamoxifen administration.

k. In Form A, item 8h, please address the following:
    i. Reconcile numbers between sections and justify group size for the various studies.
    ii. Separate expt #8 into low and high doses as high dose has only one time point.
l. In Form A, item 10a, lines 2 and 3 should be removed. Add mice with method #1 for retried breeders and excess pups.
m. In Form A, item 13a, add hyperoxia adult exposure.
n. In Form A, item 13b, searches need to be more focused for alternatives.
o. In Form A, item 14, please address the following:
    i. Update training dates for personnel #2
    ii. Clarify specifically who will conduct PA administration. These personnel must be listed in IBC protocol for this purpose.
p. In Form B, item 4, line 4, please clarify reference to IT.
q. In Form B, item 5a remove nonsurvival.
r. In Form B, item 6c1, please address the following;
    i. Tapered needle should be used for closure of peritoneum. Please reconcile for this layer.
    ii. Remove current analgesia and indicate that standard buprenorphine (0.05 mg/kg SC) will be administered immediately following surgery and a second dose will be administered at 12 hours for a total of two doses.
s. In Form B, item 6etable, class III, remove check mark from buprenorphine SR LAB.
t. In Form B, item 9, please review monitoring frequency and strains/studies to list here with ACC.
u. Breeding, reconcile with A4 and A8g/h.

7. Review from Subcommittee #2

19-150

The Committee reviewed the protocol and discussed that the PI had addressed all the clarifications requested from subcommittee and that there were no additional clarifications needed. Following discussion, a motion to approve this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

19-151

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 3, remove current funding and list the specific funding agency, grant title, grant number and funding PI for collaborator here.
b. In Form A, item 8g, please address the following concerns:
    i. Under procedure B1.3, please change the number of animals from 8 to 10.
    ii. Under "Minimization", please address the following concerns:
        1. Please change the word "specimen" to "animals".
        2. In the third paragraph, please indicate the estimated maximum time for total procedure.
        3. Last sentence change to "Ten sessions will take place with 1 animal/session used, and in each exposure of three tissues will be performed"
    iii. Under the summary of procedures, the length of times indicated per procedure/task do not match what is in Form B, item 6c. Remove all times from Form A.
c. Form A, item 14, please address the following concerns:
    i. For all personnel, under specific procedure, please indicate which procedures specific to this protocol will be done by each personnel.
d. In Form B, item 3, remove all answers and check marks as all procedures occur under a surgical procedure.
e. In Form B, item 4, please address the following concerns:
    i. Please remove Dexmedetomidine.
    ii. Please add xylazine and butorphanol to the table and review with veterinary staff as to dose.
    iii. Change the dose of Tiletamine + zolazepam to 4.4 to 6.6 mg/kg.
f. In Form B, item 6a, please add that hair will be clipped as part of surgical preparation.
g. In Form B, item 6b, please remove dexmedtomidine
h. In Form B, item 6f3, remove the answer provided. This section is N/A.
i. In From B, item 8, remove the answer provided. This section is N/A

19-154

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. Condition of Initiation: PI needs to provide a copy of CITES permit to ACC when obtained.
b. In Form A, item 4, see comments below and reconcile.
c. In Form A, item 8h, please clarify how N=24/location will result in 600 crested, 200 banded, and 200 Lau animals. For each species, list the number of locations for collection and multiple that number by N=24 and reconcile those numbers with A4.

8. Review from Subcommittee #3

19-139

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications are needed and to defer the protocol for rereview by the full committee was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 4, please reconcile the numbers listed here with those in A98g, A8h and Appendix 1.
b. In Form A, item 7a (and Hazard Appendix), 2,4-dimethoxybenzaldehyde is not a carcinogen. It appears that there is some confusion and that 7,12-dimethylbenz[a]anthracene (DMBA), should be listed as this is the agent commonly used to induce mammary cancers in rodents.
c. In Form A, item 7d2, please see comments below and only include tribromoethanol (Avertin) in this section if it can be scientifically justified.
d. In Form A, item 8c, this must be answered for work conducted in last 3 years.
e. In Form A, item 8f, please address the following:
    i. Remove "If so, we….<2."
    ii. Please indicate the following: Any breeding animals used to produce female experimental animals that develop skin inflammation or loss of body condition will be euthanized if any ulcerative dermatitis is seen.
    iii. Please indicate the following: For experimental animals, a treatment plan will be developed by the veterinary staff and carried out by the protocol staff.
f. In Form A, item 8g, please provide the following clarifications and changes:
    i. Summary table, revise table to create a column for the number of animals initially required, the number used, and the number remaining for each genotype and aim. The number remaining is the experimental number that needs to be listed in A4.
    ii. Aim 1, please address the following:
        1. Clarify what the ratio between the VDR+/+ and VDR-/- mice will be in the co-housing in Aim 1 or whether the co-housing is done with animals within the same strain.
        2. Clarify how the fecal samples will be collected.
        3. Please clarify the specific method of euthanasia for this Aim.

4. Avertin cannot be used unless it can be scientifically justified including references that show that other anesthetic agents cannot be used. If another anesthetic is used, please be sure to list agent, dose and route.
5. Delete in Aim 1 the in vitro description.

iii. Aim 2, please address the following:
1. Provide a substantial rationale for the continuous mating.
2. Change the mating scheme to 1 male and 2 females.
3. State that the breeding dams are the experimental animals and not the offspring.
4. Clarify the anticipated duration of this experiment.
5. Revise animal numbers based on groups that are already completed.
6. Remove sample collection and analysis section.

iv. Aim 3, address the following:
1. Indicate the sex of the nude mice that will be used.
2. Line 3, change "were" to "will be".
3. Line 5, correct to "MCF7 cells (10^6) in the lower left mammary fat pad percutaneously in 100 ul PBS."
4. Clarify the treatments details here.
5. Indicate the specific method of euthanasia for this aim.

v. Under Monitoring and Humane Endpoints, please address the following:
1. Indicate here: See A8f for monitoring for ulcerative dermatitis.
2. Add tumor ulceration as humane endpoint for sets 2 and 3.
3. Add the following: In addition to the monitoring outlined in this section, all animals will be monitored at least once daily by a member of the animal care staff and if any concerns are noted, a member of the veterinary staff will be consulted.

vi. Under Statistical Plan, please address the following:
1. Indicate the specific parameter assessed that was used for the effect size determination as the basis for the power analysis.
2. Delete the last sentence of the first paragraph.

g. In Form A, item 10a, line 2, please address the following:
i. See comments above and reconcile here.
ii. Column #2, this is not a method, this is a drug. Use the key and insert method number.
iii. Column #3, insert the drug and dose,

h. In Form A, item 13a, please provide the requested justification here.

i. In Form A, item 14, please address the following:
i. Please clarify who specifically will be injecting tumor cells in mammary fat pad, monitoring for tumors in these animals, and their specific expertise/training with these procedures. If none, then indicate who with expertise will train them.
ii. Under procedures, clarify what DMBA cancer model means by listing the procedures involved and specific expertise/training with

these procedures. If none, then indicate who with expertise will train them.
iii. It must be clear who is conducting the various methods of euthanasia and their expertise/training with these procedures.
iv. Personnel #3, #4, #5, and #7, correct relationship and training dates.

j. In Form B, item 3, please address the following:
i. Under gavage, do not list dose, vehicle, duration, or age here.
ii. Under "other", list human cells and SC injection in mammary fat pad and remove all other information.
iii. Under blood collection, depending on method of euthanasia proposed, if blood is collected as part of the process of euthanasia (ie cardiac puncture) then list cardiac puncture here and check yes for anesthetic. If it collected post-mortem, this will not apply.

k. In Form B, item 9, please address the following:
i. Indicate here: See A8f for monitoring for ulcerative dermatitis.
ii. Add tumor ulceration as humane endpoint for sets 2 and 3.
iii. Add daily monitoring.

l. In Form B, item 11, remove answer.
m. Hazard appendix, correct compound to 7,12-dimethylbenz[a]anthracene.

19-145

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 2b, please provide a work number for second personnel listed here.
b. In Form A, item 8g, under procedures, please indicate that different animals will be used for the sucrose splash test and sucrose preference test and insert the word "behavioral" before the word testing at the end of the section on the splash text.
c. In Form A, item 8h, please address the following:
i. Split the column "# of assays" into two columns, one for the behavioral test and one for the assays related to terminal tissue harvest.
ii. Indicate the parameter used for the means for the power calculation.
iii. Please clarify why 6 males and 6 females are requested while the required sample size is calculated at 12/group. Please indicate if PI anticipates sex differences.
d. In Form A, item 9, please indicate discarded or saved and the method of storage if saved.

19-149

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. General Comment: IBC protocol must be modified and approved for use of these viruses in animals prior to final approval of this protocol.
b. In Form A, item 2b, please provide an emergency phone number for personnel listed in column #1 and #2.
c. In Form A, item 2b, under role on protocol, for both personnel remove answer and list #1.
d. In Form A, item 3, remove grant as this grant is not approved for animal work.
e. In Form A, item 4, please indicate units for column 5 (i.e., weeks).
f. In Form A, item 5c, remove line 2 as euthanasia must occur in biohazard room listed on line 1.
g. In Form A, item 6b, please correct or provide a justification for opting out.
h. In Form A, item 6f, please uncheck the yes box and check no or provide a justification, indicate which specific animals, and when this is required.
i. In Form A, item 7a, please address the following:
    i. Line 2, list specific viruses and bacteria to be used.
    ii. Lines 3-5, check no.
j. In Form A, item 7c, please indicate active charcoal scavenging for this room.
k. In Form A, item 8b, please provide one or more references that the human herpes viruses that will be studied in this protocol will lead to infection in mice, as herpes viruses tend to be very species specific in their pathogenicity.
l. In Form A, item 8e, please delete the prefix "anti-" in the third line.
m. In Form A, item 8g, please address the following:
    i. Provide a reference for the greater sensitivity of female mice to both bone loss and infectivity as compared to male mice and whether this is true for all agents
    ii. In study design, indicate that the ligatures used are silk.
    iii. Indicate the disposition of animals that will be excluded because of ligature dislocation.
e. In Form A, item 8h, please address the following:
    i. Sample size justification is for N=6, but as PI is euthanizing two animals at day 2 and 4 at day 18, the group sizes are 2 and 4 and not 6. Please revise justification.
    ii. Indicate a modification will be submitted if studies need to be repeated.
n. In Form A, item 10c, please uncheck the box.
o. In Form A, item 13a, indicate that model is less invasive than other models and reproducible.
p. In Form A, item 13b, please add alternatives to the search terms.
q. In Form A, item 14, please address the following:
    i. Personnel #1, under training and expertise, please remove "Dissection and…tail-vein injection" as this is not relative to this

protocol or is post-mortem and indicate expertise with the ligature procedure.

ii. Personnel #2, under procedures, remove "collection ….bone" and under training and expertise, identify the training and expertise of all individuals please remove "Dissection and…tissues" as these are post-mortem. Under training and expertise, indicate expertise with the ligature procedure.

19-152

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 7d2, please address the following:
   i. Please provide the scientific justification using a number from the list of common justification scenarios following the table for each compound rather than stating "same as above" as this is clearly not correct.
   ii. Provide the requested information storage for all compounds.
   iii. Remove the cells as these are not compounds.
   iv. For the last compound listed, please clarify the vehicle, whether the compounds and vehicle come sterile and the storage conditions.
b. In Form A, item 8g, please address the following:
   i. Provide indicate that the maximum # of implants per animal is 4 and that they will be placed in one of the four quadrants on the back.
   ii. Please indicate the specific fluorescent compound used, the vehicle, and the volume.
   iii. Please clarify what the longest duration of the experiments will be.
   iv. Please indicate one or more references for this established model.
f. In Form A, item 8h, please address the following:
   i. Please clarify why both males and females can be used. In the vasculogenesis study, only males will be used which is justified for that study, but it is not clear why both sexes are used for osteogenesis and chondrogenesis studies. Would it not be more appropriate to use one sex for the osteogenesis and chondrogenesis parts of this pilot study to avoid sex influence and then in the future request additional animals of other sex for a full study? In addition, if both males and females will be used, please clarify if they will be used in equal number for each experiment.
g. In Form A, item 10a, please change the method from 2 to 1 and remove answer from 3rd column as this is not required for method #1.
h. In Form A, item 10c, please uncheck the box.

i. In Form A, item 13b, the first search should have listed 112 references. Please reconcile.
j. In Form A, item 14, correct training dates
k. In Form B, item 6c, surgery #1, please address the following:
    i. Please correct to monofilament sutures for skin sutures and indicate when they will be removed.
    ii. Reconcile the maximum volume of the construct implants listed here with A8h.

19-135

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review via a subcommittee of members 6 and 10 following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, page 1, please list the old protocol number in the correct location and the new number in the correct location on the form and in in the header on all other pages correct the number to the new protocol number.
b. In Form A, item 4, please reconcile these numbers with those listed in item 8g and Breeding form.
c. In Form A, items 5b and c, please contact veterinary staff to clarify which rooms will be used for AOM and DSS.
d. In Form A, item 5c, please remove administration of DSS in the same location as AOM and indicate location identified by veterinary staff for this purpose.
e. In Form A, item 6d2, change "Pedialyte" to "electrolyte solution"
f. In Form A, item 7a, please check the no boxes in the last four categories.
g. In Form A, item 7d2, please address the following:
    i. Line 1, it is suggested that saline instead of distilled water be used the vehicle for this compound.
    ii. Line 3, column #1, remove "pedialyte" with "electrolyte solution" and indicate the source of the various components of that solution.
h. In Form A, item 8a, rewrite the text in more layperson's language indicating importance to human health.
i. In Form A, item 8d, please explain in the text why culture or computer models are not useful.
j. In Form A, item 8e, please provide the genetic background of the APCflox and DRA-/- mice.
k. In Form A, item 8f, please provide information about the DRA-/- mice that develop complications.
l. In Form A, item 8g, under humane endpoint criteria, please clairyf the following:
    a. Under AOM model, please address the following:
        i. Please indicate the age of mice when AOM will be administered.
        ii. Please clarify what the 9-10 weeks time point is in reference to. Is this after the AOM injection or after DSS treatment which will last 9 weeks is completed.

iii. Please clarify that animals will be weighed daily during DSS treatment and will continue to be weighed daily if >5% weight loss is noted when DSS is stopped. Please clarify monitoring and weighing frequency once DSS cycles end until the end of the study.
iv. Under humane endpoints and monitoring, include severe diarrhea as an endpoint.

m. In Form A, item 8h, please provide the following clarifications and changes:
   i. Single time point experimental design will not allow for determination of rapid development. Delete from this section.
   ii. Clarify how many DRA-/- animals are expected to develop severe diarrhea, whether they will be excluded, and whether such losses are taken into account in determining the numbers of animals requested.
n. In Form A, item 13b, please address the following:
   i. Please update search for DRA.
   ii. Remove search for Olfr-78 as this is not relative to this protocol.
o. In Form A, item 14, add under procedures that administration of electrolyte solution in drinking water for all personnel responsible and change pedialyte to electrolyte solution.
p. In Form B, item 3, please clarify whether other biologic samples will be collected and reconcile with A8g.
q. In Form B, item 7, include the DSS model component in this section and indicate the frequency with which animals will be observed and weighed while on DSS and end point criteria that would result in removal of the animals from study.
r. In Form B, item 9, please write two paragraphs, one for AOM/DSS model and one for genetic model and include DRA diarrhea phenotype in the monitoring and humane endpoints.
s. For Breeding form, reconcile the numbers of animals with A4 and A8g/h.

9. Report of Designated Review(s), Exemptions, and Lab Visits

a. Protocols

19-146

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In In Form A, item 4, line g, add C57 mice, males, 360 <4 weeks, and use #3 to account for males born and not used.
b. In Form D, item 14, PI needs to update online ACC Regulatory training. .

19-148

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 5a, please check [redacted] location for transgenic zebra fish are currently being maintained.
b. In Form D, item 14, personnel need to update ACC Regulatory Training and correct training dates.

b. Exemptions

Member 6 indicated that there was one protocol requesting continuation of partial exemptions from the UIC Environmental Enrichment Plan this month. The Committee reviewed the request and a motion to approve continuation of the request was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

18-170 The PI of this protocol has requested a partial exemption from the UIC Environmental Enrichment Plan. More specifically, the PI is requesting exemption from housing animals with social contact (both direct and indirect through mesh panels) following infection of animals with Mtb. The rationale behind the request is to prevent spread of infection between animals and/or different study groups of animals. The exemption is only for the post-infection time-period.

c. Lab Visits

Member 6 directed the Committee's attention to the laboratories that were visited as part of the post-approval monitoring program.

Lab	ACC
[redacted]	17-018, 18-110 18-086, 18-176 19-062 17-074, 17-102, 17-182 18-171, 18-194, 19-026

10. New Business

a. Review of Guidelines/Policies/Plans

The Committee reviewed the following policies, guidelines and plans: Nonpharmaceutical Grade Compounds, Use of Expired Medical Materials, Use of Wire-Bottom Caging in Rodents, Use of Urethane in laboratory animals, Exercise Plan, Enrichment/Social Housing Plan, Social Housing and Adoption. Following discussion

that the NPG and adoption policies did not require any changes, and that the remainder of the policies, guidelines or plans were updated for current format and a reference update, a motion to approve was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

b. Modification of Protocol 17-154 Mod 04

The Committee reviewed the PI's request for the following: 1) Change in species from rats to mice, 2) Addition of IP injection of hypertonic (1.5 M) saline to induce thirst alone or in the presence of losartan, an angiotensin II antagonist or isotonic saline +/- losartan as a control to assess behavior associated with thirst, 3) Addition of SC injection of diuretic forsemide to animals on ad libitum water and Na deficient diet for 24 hours +/- losartan or SC normal saline on ad libitum water and Na deficient diet for 24 hours +/- losartan to study sodium depletion behavior. All mice will be tested with two-bottles for 1 hour during laboratory (distilled water or 0.45 M NaCl). The Committee discussed that the PI needed to clarify the following: the strain, justification for group size, the maximum number of times animal would be used and final disposition and total numbers for class, reference to original protocol, cage labeling and irradiated diet, correct chow type, correction NPG rationale, and that new personnel needed to update training. Following discussion, a motion that clarifications were needed with designated member review following full committee for this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Modification of Protocol 18-247 Mod 01

The Committee reviewed the request for a change in PI as the original PI has left UIC and the new PI will be taking over the grant and for the addition of personnel. The Committee discussed that the PI needed to clarify the following: remove information related to funding as this was on protocol already and procedures with animals to be conducted by PI. Following discussion, a motion that clarifications were needed with designated member review following full committee for this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

d. Modification of Protocol 18-232 Mod 03

The Committee reviewed the PI's request for addition of surgery for SC implant to osmotic pump for administration of nicotine or DREADD activating agent. The Committee discussed that the PI needed to clarify the following: the rationale for the request for both nicotine and DREADD activating agent and justify why it is needed, change O2 to medical grade air, clarify fine tuning and training animals, provide pump model, dimensions, dose, and rate of administration, indicate surgeons and training, indicate veterinary consult for dehiscence or infection complications, and conduct literature search for alternatives. Following discussion, a motion that clarifications were needed with designated member review following full committee for this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

e. Modification of Protocol 18-209 Mod 01

The Committee reviewed the PI's request addition of 231 FVB for testing a syngenic model of ovarian cancer STOSE cells to determine if CXCR1 antagonists increase efficacy of PARP inhibitors and to characterize the native immune system response following treatment with CXCR1 antagonists. The Committee discussed that the PI needed to clarify the following: revise title, indicate route, number of cells and volume and remove reference to PDX and visible for experiment 3, clarify that required for experiment 5 was to switch strains, and provide murine pathogen test results for cell line. Following discussion, a motion that clarifications were needed with designated member review following full committee for this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

f. Modification of Protocol 18-035 Mod 01

The Committee reviewed the PI's request for changing from ZPI KO/Fix KO to ZPI KO/FVIII KO, for addition of testing recombinant proteins in hemophilia model, addition of tail vein rebleed assay, adding of tail vein snip survival assay, addition of hemathrosis model, addition of tail vein blood collection, and addition of CCTS funding. The Committee discussed that the PI needed to clarify the following: conservation of FIX and FVIII between murine and human, rationale for transection assay, move tail vein blood collection to correct location on form and remove analgesia for this procedure. Following discussion, a motion that clarifications were needed with designated member review following full committee for this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

g. Modification of Protocol 17-061 Mod 19

The Committee reviewed the PI's request for use of two animals for testing M3mP6 for bolus and 24 hour infusions to determine MTD. The Committee discussed that the PI needed to clarify the following: additional monitoring time points for group 2, dosing of one animal at a time, and removal of reference to rat dosing. Following discussion, a motion that clarifications were needed with designated member review following full committee for this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

h. Modification of Protocol 18-024 Mod 03

The Committee reviewed the PI's request for the following: 1) 272 additional mice for addition of ethanol conditioned place preference test and for conditioned place aversion test to test if manipulation of perineuronal nets affects the rewarding and aversive properties of ethanol. PNNs will be "digested" by administration of chondroitnase ABC via stereotaxic injection, 2) change in current aversion-resistant ethanol consumption procedure to allow for testing various concentrations of quinine with ethanol due to females being more resistant to quinine, and 3) addition of personnel. Following discussion, that the addition of these tests and change in test were appropriate to the

protocol and that there were no concerns, a motion to approve this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

i. Modification of Protocol 19-048 Mod 01

The Committee reviewed the PI's request to clarify monitoring frequency and discussed that this would increase to daily once SC tumors reach 1.0 cm. Following discussion that there were no concerns, a motion to approved this modification was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

ANIMAL CARE COMMITTEE MEETING MINUTES
OCTOBER 15, 2019

Attendees: Member 6, Member 8, Member 9, Member 10, Member 11, Member 24, Member 30, and Member 41 (for member 2)

Absent: Member 2

Guest: None

1. **Minutes**

Minutes were sent for designated review determination.

2. **Announcements**

Member 9 informed the committee of addition of 1 item under new business as item p.

3. **Old Business**

   a. **SCAW Workshop**

Member 9 informed the committee regarding the upcoming SCAW meeting and registration deadlines.

4. [redacted] **Director's Legislative and Facility Update**

The Committee discussed the following 1) that the annual USDA animal usage requests were sent out last week to collect data for annual report that is due by December 1st of this year; 2) that [redacted] is in the process of upgrading animal facility security systems following a security audit by UIC police, and 3) that a member of veterinary staff and a member of the investigator's lab took part in a 4 -ay long gnotobiotic course that provided hands on training on working with gnotobiotic isolators.

5. **OACIB Update**
   a. **Modification**

Member 9 updated the Committee to the following activity during the past month: there were 2 modifications approved via administrative level, 27 modifications approved administratively following veterinary consult, and 19 modifications approved via designated review this month. In addition, there were 20 protocols that added personnel, 0 with personnel deletions, 0 that added new funding, and 0 in which animals were added to the holding protocol.

b. Continuations and Terminations

Member 9 directed the Committee's attention to the protocols for continuation and those terminated due to expiration or PI's request. . The Committee discussed that all protocols had completed the appropriate continuation documents and a motion for designated member review for renewal the protocols was passed by the following vote: 8 in favor, 0 opposed, 0 abstention, and 0 recusals.

6. Review from Subcommittee #1

19-160

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 2b, role on protocol for personnel listed in third column indicates that role is "hands-on", but they are not listed in Form A, item 14. Either correct role here or include in A14.
b. In Form A, item 5c, please clarify if animals will be maintained in [redacted] for up to 23 hours post-surgery and then returned to [redacted] and if so [redacted] should be designated as study area and added as location to item 5d.
c. In Form A, item 5d, please add [redacted].
d. In Form A, item 7d2, according to A8a, as mannose is incorporated into some of the preparations, please include this agent in this section. In addition, please indicate what the vehicle is for administration.
e. In Form A, item 8d, please add a statement to indicate that the type of tissue damage caused by MI model cannot be studied in vitro.
f. In Form A, item 8g, please address the following:
    i. Under procedure #1, please address the following:
        1. In first paragraph, please clarify if the sham and/or MI/R untreated group will receive vehicle as control.
        2. In 2nd paragraph, please address the following:
            a. Please indicate the dose of nanoparticles to be administered.
            b. In the second sentence please add "or vehicle" if vehicle will be used.
    ii. Under procedure #2, please address the following:
        1. In first paragraph, please clarify if the sham and/or MI untreated group will receive vehicle as control.
        2. In 2nd paragraph, please address the following:
            a. Please indicate the dose of nanoparticles to be administered.
            b. In the second sentence please add "or vehicle" if vehicle will be used.
        3. In the last paragraph, please address the following:

a. Please change ANP to M-ANP and PANP to M-ANPs.
b. In line 4, change 4 week to 2 week.

iii. Please create a new section for humane endpoints and monitoring and remove from the end of IVIS paragraph, remove lack of purposeful movement upon stimulation and add severe lethargy and body condition score of less than 2.

g. In Form A, item 8h, please address the following:
   i. Under expt #1, please address the following:
      1. Please state what effect size was used for power analysis and remove "is needed".
      2. Please state which pressure volume loop procedure will be used for this experiment.
   ii. Under expt #2, please address the following:
      1. Please state what effect size was used for power analysis and remove "is needed".
      2. At the bottom of the paragraph correct the numbers to 185 each and total of 370.
h. In Form A, item 10a, line 1, column #2, please change to #2.
i. In Form A, item 10c, check cervical dislocation.
j. In Form A, item 13a, please address the following:
   i. Please clarify the significance of testing both the MI and I/R models. Why are both models needed?
   ii. Please list both PV loop procedures, justify both, and clarify why both are needed.
k. In Form A, item 13b, conduct literature search for alternatives to acute surgical procedures.
l. In Form A, item 14, please address the following:
   i. Please see comment "a" above and reconcile. In addition, please note that this person must update his "Animals and Research at UIC" training.
m. In Form B, item 6b, please address the following:
   i. Remove ketamine/xylazine/acepromazine as all animals will be under isoflurane anesthesia and undergo cervical dislocation at the end of PV loop procedures prior to tissue harvest.
   ii. Please clarify that anesthetic regimen is for MI and I/R,.
   iii. Add etomidate administration to both MI, I/R surgery and to P/V surgery.
n. In Form B, item 6c, surgery # 2, please clarify that during 45 minute ischemic period animals will be continuously monitored.
o. In Form B, item 6c, surgery #3, please address the following:
   i. Please remove time points and reference to TAC, as these do not agree with A8g and indicate the following: "At time points indicated in A8g following MI or I/R, mice will be….".
   ii. Please indicate that following completion of P/V surgery, animals will be euthanized by cervical dislocation prior to tissue harvest.
   iii. Under P/V-Right Ventricle, reconcile method of euthanasia with A8g.
   iv. Remove last two sentence.

p. In Form B, item 9, please revise humane endpoints to respiratory distress, severe lethargy and body condition score of less than 2 and remove other endpoints.

19-163

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 3, Funding #1- 3, update institutional #'s and check funding status for #3.
b. In Form A, item 4, please address the following:
    i. Number of experimental animals does not agree with A8g/h or Breeding form. Please reconcile.
    ii. Please add "ERT" to the Cre mice nomenclature when using are Cre-ERT strain. This needs to be consistent throughout the protocol.
    iii. Please clarify the ages of experimental animals. These are not consistent with the A8g. For example, for diet studies in which animals are on diet for 2 or 6 months. The mice must be at least one month old before they can go on study and some must be administered tamoxifen for a period of time prior to starting study; therefore the 2 and 6 month ages listed are not correct. Moreover, there are other studies that do not have two ages listed, but two ages are listed in the table for experimental animals. Please reconcile.
c. In Form A, item 6g, uncheck as this is N/A.
d. In Form A, item 8a, define dyslipidemia in lay terms.
e. In Form A, item 8b, define AFM, FIV, and NO as first use.
f. In Form A, item 8e, please address the following;
    i. Please include discussion of crossing mice with Tie2-Cre-ERT and Chd5-Cre-ERT (Ve-cad-Cre-ERT) for tissue specific inducible KOs.
    ii. Remove the last two sentences.
g. In Form A, item 8g, please address the following:
    i. Under Study design for dyslipidemia-induced endothelial stiffness, please address the following:
        1. Please clarify that the jugular injection is a percutaneous injection.
        2. Please clarify when tamoxifen administration is initiated in relation to the start of diet treatments.
        3. Please add "ERT" to the Cre mice nomenclature when referring to the Cre-ERT strain.
        4. For tamoxifen treatment column please clarify when there is only one group if this is + or – tamoxifen.

5. Please clarify briefly what is done with the primary endothelial cells and if these are from naïve (no special diet) and the age of the mice.

ii. Under role of Kir channels, please address the following:

1. Please clarify briefly what is done with the primary endothelial cells and the age of the mice.
2. The table for study 1B has a formatting error and the table does not print correctly. Note; this does not show up online. Please redo the table.
3. Table for 1C dose not line up. Please correct.
4. The table for study 2 has a formatting error and the table does not print correctly. Note; this does not show up online. Please redo the table.
5. Under Study 3, please clarify briefly what is done with the primary endothelial cells and the age of the mice.

h. In Form A, item 10a, line 1 and 2 column #3, remove percentage. For CO2, this should be left blank.

i. In Form A, item 14, please address the following:

i. Please ensure that all personnel are listed here.

ii. PI should only be listed in this section if hands-on with animals.

j. Breeding form, see comments above and reconcile total numbers with A4 and A8g/h.

19-165

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 2b, PI should check "Yes" for copy of correspondence to second project staff.

b. In Form A, item 4, committee suggests that PI obtain 4 week old animals and start the experiments at 5 weeks of ages as this will minimize problems associated with weaning, transportation stress and new facility and diet.

c. In Form A, item 6e, should be completed for 60% high fat diet feeding.

d. In Form A, item 7c, PI should check "Yes" for the use of isoflurane for excisional skin wounding as described in A8g. Also indicate location for use and method of scavenging isoflurane.

e. In Form A, item 8b, please provide references in regards to role of histone acetylation in obesity induced inflammation and wound healing as indicated.

f. In Form A, item 8g, please address the following:

i. Under "establishing type 2 diabetes, committee suggests that PI obtain 4 week old animals and start the experiments at 5 weeks of age, please correct accordingly.

ii. PI should include a reference for 10 weeks of 60% high fat diet-induced type 2 diabetes. PI should also indicate the proportion of mice that develop type 2 diabetes using this treatment regimen? If the incidence is less than 100%, then

all animals should be tested for type 2 diabetes. In addition, PI should include blood glucose criteria for type 2 diabetes.

iii. PI should remove monitoring criteria of >20% weight loss.

iv. Under treatment, the volume for oral administration should be 5 ml/kg.

v. Since the PI is establishing the diabetic wounding model for the first time in his lab, the committee requests that the PI include a second control group which will receive analgesic treatment to determine whether the use of analgesics in this study will effect wound healing and provide update following study.

g. In Form A, item 10a, the committee suggests that PI change method of euthanasia to isoflurane (method #5) and check the appropriate box in A10c.

h. In Form A, item 13a, 2nd sentence, the statement regarding the size of the animal should be removed.

19-166

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. General Comment: PI needs to clarify why the studies cannot be combined into a single set of animals in one species.

b. In Form A, item 4, see comment above and reconcile for total.

c. In Form A, item 5c, please clarify housing after animals have been to MRI or removed from [redacted]. What specific room in [redacted] are animals housed in?

d. In Form A, item 7c, add MRI location here and list active charcoal scavenging.

e. In Form A, item 8a, please address the following:

   i. Define HHCC.

   ii. Clarify the specific source of the two chimeric cells. A8b refers to human chimeric cells from cord blood. If this is the source then it must be clear how these cells differ from HUCC cells in ACC 19-167.

f. In Form A, item 8e, see comments above related to species and if rats will be used, then justify the specific strain.

g. In Form A, item 8g/h, please address the following:

   i. See comment above and reconcile.

   ii. Under general study design, please address the following:

      1. Under #1, this section states that MRI will be prior to cell administration and at end of study, but under #2, day 30 MRI is also indicated.

      2. Under #1, blood collection via cardiac puncture is indicated. Please clarify if this is after euthanasia or if it is prior to euthanasia. If prior to euthanasia, then provide details as to how depth of anesthesia is assessed prior to collection.

      3. Under #2, the 2nd paragraph indicates weekly blood collection. Please describe the specific procedure used,

whether anesthetic is used and if so, indicate specific drug and dose, and indicate volume of blood collected.

iii. Under intraosseous injection, line 9, change "dosed" to "closed".
iv. Under intravenous and subcutaneous, indicate maximum volume injected.
v. PI needs to clarify the high attrition rate and what the complications are that warrant 20% additional animals.
vi. Clearly state the signs of toxicity that will be assessed.

h. In Form A, item 13c, remove answer if no alternatives were found.
i. In Form A, item 14, please address the following:
    i. For personnel #1, only list in this section if PI will be hands-on with procedures.
    ii. For personnel #2, please clarify specifically for IV injection tail vein and jugular and clarify expertise with both routes.
j. In Form B, item 3, change IV injection to IV RO and IV percutaneous jugular.
k. In Form B, item 4-6, see comments above about use of two species and update if applicable.

19-167

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. General Comment: PI needs to clarify why the studies cannot be combined into a single set of animals in one species.
b. In Form A, item 4, see comment above and reconcile for total.
c. In Form A, item 5c, please clarify housing after animals have been to MRI or removed from [redacted]. What specific room in [redacted] are animals housed in?
d. In Form A, item 7c, add MRI location here and list active charcoal scavenging.
e. In Form A, item 8e, remove reference to "nude NSG" mice. NSG mice are not nudes.
f. In Form A, item 8g/h, please address the following:
    i. See comment above and reconcile.
    ii. Under general study design, please address the following:
        1. Remove the references to nude mice and replace with NSG.
        2. Under #1, this section states that MRI will be prior to cell administration and at end of study, but under #2, day 30 MRI is also indicated.
        3. Under #1, blood collection via cardiac puncture is indicated. Please clarify if this is after euthanasia or if it is prior to euthanasia. If prior to euthanasia, then provide details as to how depth of anesthesia is assessed prior to collection.
        4. Under #2, the 2nd paragraph indicates weekly blood collection. Please describe the specific procedure used,

whether anesthetic is used and if so, indicate specific drug and dose, and indicate volume of blood collected.

iii. PI needs to clarify the high attrition rate and what the complications are that warrant 20% additional animals.
iv. Clearly state the signs of toxicity that will be assessed.
v. Study II, change HHCC to HUCC.

g. In Form A, item 13c, remove answer if no alternatives were found.
h. In Form A, item 14, please address the following:
    i. For personnel #1, only list in this section if PI will be hands-on with procedures.
    ii. For personnel #2, please clarify specifically for IV injection tail vein and jugular and clarify expertise with both routes.
i. In Form B, item 3, change IV injection to IV RO and IV percutaneous jugular.

19-168

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that significant clarifications are needed and to defer the protocol for re-review by the full committee was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. General Comment: The overall goals of this protocol are not clear. It is not clear if schizophrenia will be studied, if schizophrenia + alcohol addiction will be studied, or if PNR is just being used as a stressor to determine if this predisposes animals to addictive behaviors. Moreover, the rationale for inclusion of autism model mice is not clear. A8a and A8b need to be rewritten so that the goals are clear and the background is clear. In addition, the searches provided in A13b should match the goals.
b. In Form A, item 2b, emergency numbers for all personnel listed here need to be provided.
c. In Form A, item 3, remove PPG as the specific project proposed with rats is not currently covered in this protocol.
d. In Form A, item 4, the # of C57 mice needs to be indicated and PI also needs to account for intruder mice. Based on revisions, other numbers may need to be reconciled.
e. In Form A, item 6b, please clarify this request and this section refers to sucrose splash test and sucrose preference tests that are not part of this protocol. Either remove request and uncheck exemption from enrichment or provide appropriate justification.
f. In Form A, item 6c, please add single housing for mice that will be on two bottle ethanol studies.
g. In Form A, item 6d2, this section needs to be completed for ethanol in water and the Lieber DiCarli diet.
h. In Form A, item 7d2, column #2, remove answer and list either 2 or 3 (see key provided) for justification and #1 for RG-108.
i. In Form A, item 8a, please address the following:
    i. The PI has added extra b and c heading in this section and this has mislabeled all other parts of section 8. Please correct.

ii. A8a and A8b (currently d), see general comment above and rewrite these sections.

j. In Form A, item 8e, please address the following:
   i. Please clarify the justification of each strain of mice as it relates to alcohol studies and for other studies proposed in this protocol including BTBR mice.
   ii. Please justify SD rats.

k. In Form A, item 8g, please address the following:
   i. Under PNS, please clarify the last paragraph that states that this will be developed in SW mice, as PI has been using this model for several years.
   ii. Please clarify the reference to "characterizing the phenotype" as PI has already characterized the model and published on it.
   iii. Under drug administration, please clarify the following:;
      1. Please clarify when behavioral testing starts in relation to drug administration.
      2. Please clarify the concern that several tests are run on same mice on different days; therefore, the timing as to end of drug administration and start of testing will be different for various tests.
      3. Please clarify the reference to rat studies being confirmatory as the studies proposed in rats are not the same models as proposed in mice.
   iv. Under two bottle test, please address the following:
      1. This section states that this will be done in adult male mice from PNS or NS moms, but study 1 states that the exposure to ethanol is prenatal to dam and that both sexes will be studies. This must be reconciled.
   v. Study 1a, please address the following:
      1. Please see comment above and reconcile time of alcohol exposure.
      2. Please clarify if there should be two groups for ethanol, ethanol +NS and ethanol +PNS.
   vi. Study 2, the goal of studying alcohol in autism mice needs to be clarified.
   vii. Study 3, the specific drug or drugs to be used and the doses need to be clarified.

l. In Form A, item 10b, check cervical dislocation.

m. In Form A, item 10d, uncheck box.

n. In Form A, item 13b, please revise search if schizophrenia is not part of this protocol.

o. In Form A, item 14, please address the following:
   i. The personnel must update online Regulatory training.
   ii. Remove procedures that are not part of this protocol from this section.

p. In Form B, item 3, add oral gavage.

19-155

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item A2a, please remove the check mark from "new address".
b. In Form A, item A2b, please correct role on protocol.
c. In Form A, item 4, please address the following:
    i. Reconcile the numbers to what is indicated in A8g.
    ii. For NSG-SGM3 remove breeding.
d. In Form A, item 7d2, please address the following;
    i. Please include the details for clodronate liposomes
    ii. Change scientific justification for IMDM to #1
e. In Form A, item 8b, define CMA.
f. In Form A, item 8g, please address the following:
    i. Remove 'Jak2 inhibitors', as none of the proposed experiments involve this compound.
    ii. Remove the section of the first paragraph that gives details of the two transgenic mice species and remove the strain specific details regarding nu/nu mice, as these are not required in this section and should be covered in A8e.
    iii. Under ' hematopoietic' reconstitution potential of CMA-expanded HSC' please remove the word 'excessive' and state '>20% weight loss from baseline'.
    iv. Under proposed experiments, section 1, line 5, replace 'three' groups with four groups.
    v. Under proposed experiments, section 2, please address the following:
        1. Please clearly indicate if the platelets will undergo any manipulation prior to transplantation
        2. For the main study start the description by defining the four groups involved (remove the groups from line 5)
        3. Indicate how clodronate liposomes will be delivered the mice.
    vi. Under proposed experiments, section 3, please address the following:
        1. Please change the time-point in the text for the first dose of CMA to 4 weeks, as shown in the timeline
        2. Please change the time point of peripheral blood collection in the text to 7-12 weeks as shown in the timeline.
        3. For serial transplantation, please indicate that the mice will undergo 'sub lethal dose of total body irradiation'.
        4. On page 6, first paragraph please verify the dose of TSA (0.005 ng/kg).
    vii. Under proposed experiments, section 4, please remove 'monitoring frequency will be increased if any signs of clinical illness are detected' at the first place. Under proposed experiments, section 5,

remove 'pilot study' as this is inconsistent with the justification provided for the number of mice requested for this study in A8h.

g. In Form A, item 8h, please address the following:
    i. Please indicate if equal number of male and female mice will be used or they will be used interchangeably
    ii. Indicate the total number of NSG mice requested in item 2 c) the animal numbers in this section does not match with A4. Please reconcile.
h. In Form A, item 13b, the search should also be done utilizing search terms "5 azaD, TSA, VPA, leukemia".
i. In Form A, item 14, please update the training dates and clarify who will conduct blood collection via by tail nicking and RO puncture.
j. In Form B, item 5d, uncheck the boxes as no surgery is involved.

19-158

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via a subcommittee of members 2 and 6 for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2b, please replace 'scientist' with #1 in column 1.
b. In Form A, item 5b, please specify the study that will be conducted in the chemical hazard room and uncheck the box for [redacted] biohazard room.
c. In Form A, item 5c, please indicate the marijuana extract and 4 nitroquinoline-N-1-oxide treatment and euthanasia in the procedures for the chemical hazard room and remove all information from line 1. Also, include [redacted] as a performance site for euthanasia.
d. In Form A, item 8a, please remove the experimental design language from this section and state the objectives only in lay language.
e. In Form A, item 8g, please address the following:
    i. Replace 'burder' with burden in first sentence of this section.
    ii. Please clarify # of animals requested for placebo group. As written, 40 are requested. If 40 are needed, then please justify.
    iii. Under A treatment plan - clarify the time line for the ME group, i.e. are mice receiving ME for 6 weeks and then 4NQO beginning at 6 weeks for a 10-week period (total of 16 weeks of agent delivery)?
    iv. Under A treatment plan – clarify if placebo and 4NQO and ME and 4NQO are administered at the same time/day.
    v. Under procedure description clarify if drugs are being administered on the same day or on alternate days.
    vi. Under ME administration description remove reference to "4NQO".
    vii. Add a section into A,8,g called "tumor kinetics" and indicate based upon PI's prior experience and/or the literature the kinetics of oral tumor development om the 4MQO tumor model as well as severity in terms of extent of and size of the tumors.

viii. Under assess tumor burden – clarify if PI will be able to use venier calipers in alive mice to assess tumor size.
ix. Under method of euthanasia remove "(mice<200 gm)"
x. There is a difference between study endpoint and humane endpoints. The study endpoint should be a set time based upon the tumor kinetics of the 4NQO oral cancer model. Please remove from item "a" reference to what is considered humane endpoint criteria.
xi. Under humane endpoints – remove the all the text and replace with the following: "Should animals reach humane endpoints prior to the experimental endpoint of 28-weeks mice will be euthanatized as indicated above. Humane endpoint criteria include – greater than 20% body weight loss, a body condition score < 2 on a scale of 5, tumor mass greater than 2 cms respiratory distress, pallor, sever lethargy, and active/continually bleeding tumors with ulceration and/or necrosis."

f. In Form A, item 8h, please address the following:
i. Please remove references to this being a pilot study as PI has provided statistical analysis. If this is a pilot, then number of animals requested must be significantly reduced and the statistics provided removed.
ii. Please provide justification of numbers with the adequate statistical analysis. The study design does not support a paired T-test and the power of 0.56 is very low
iii. Please indicate if equal number of male and female mice will be used or they will be used interchangeably.

g. In Form A, item 10a, Indicate [redacted].
h. In Form A, item 12a, please check "No".
i. In Form A, item 13a, please provide justification as to why the use of this method is necessary for the study and remove the last two sentences.
j. In Form A, item 13b, the search should be refined to include 4NQO, oral cancer, marijuana extract oropharynx carcinoma, 4NQO cell culture models.
k. In Form A, item 14, indicate the training and expertise for personnel listed with the procedures in this study.
l. In Form B, item 3, remove the check marks from anesthesia column if no procedure is conducted.
m. In Form B, item 7, remove all text from this section.
n. In Form B, item 9, replace what is in this section with the following: "Should animals reach humane endpoints prior to the experimental endpoint of 28-weeks mice will be euthanatized as indicated above. Humane endpoint criteria include – greater than 20% body weight loss, a body condition score < 2 on a scale of 5, tumor mass greater than 2 cms respiratory distress, pallor, sever lethargy, and active/continually bleeding tumors with ulceration and/or necrosis. In addition, indicate the frequency with which the mice will be observed and weighed. During the tumor indication phase (1st 16 weeks) animals will be observed 3 times a week due to treatment; however PI also needs to indicate freq. of observation during the rest phase and the freq. with which mice will be weighed and or tumors measured.
o. Hazard form should only address the use of 4NQO.

7. Review from Subcommittee #2

19-161

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 6c, please address the following:
    i. In first paragraph please indicate the single housing is only for rats.
    ii. In 2nd paragraph please indicate that single housing is only for 7 days post-surgery not the duration of study.
b. In Form A, item 6d2, please provide reference for water treatment.
c. In Form A, item 6d2 and 6d3, please indicate that room log will document food and water checks and dates for ad libitum feeding and daily water are provided.
d. In Form A, item 7d2, please indicate the storage condition for the compounds listed, since they will be prepared weekly.
e. In Form A, item 8b, please justify why both rats and mice are needed for model development.
f. In Form A, item 8e, please justify why only males are requested.
g. In Form A, item 8g, please address the following:
    i. For rat studies, please move the experimental design table to the beginning of the section (2nd paragraph). The table has all the necessary information regarding the study design and the assessments and the study time lines so 3rd paragraph info can be scaled back.
    ii. In Paragraph 4, please replace the blood collection time line "hallway through the study" with actual days indicated in the table.
    iii. In Paragraph 5, please clarify what are specific signs related to NASH.
    iv. In Paragraph 6, please move the following sentence "Heart, liver, and other tissue samples may be retained for future analysis at the conclusion of the experiment" to the end of this paragraph.
    v. In the rat study design table, please clarify if groups 3, 4, 5 and 6 will get euthanized after 1 week (according to the study time line) or 2 weeks (according to study design table (day 56). Please correct accordingly in both places.
h. In Form A, item 8h, correct the number of requested animals to include only 10-20 % extra animals and correct the numbers accordingly in Form A, item 4 and in item 8h.
i. In Form A, item 11, please remove the answer.
j. In Form B, item 4, please add Buprenorphine SR, proparacaine (0.5%) and bupivacaine to the table.
k. In Form B, item 6c, Surgery #1, please clarify how body wall is closed.
l. In Form B, item 6d4, please change enrofloxacin treatment to Pre-op as indicated in item 6b.
m. In Form B, item 7, please move the answer to B9.

n. In Form B, item 9, please include the following humane endpoint criteria for the animals in which NASH will be induced: severe lethargy, hunched posture, icterus, body condition score < 2 on a scale of 5 and > 20% body weight loss. Also, include freq. of monitoring and weight assessment in this section.

8. Review from Subcommittee #3

19-157

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 4, please clarify the sex (m/5), age/weight, and number of mice on line d. and remove KO from lines h and k. And please clarify why some groups consist of only males and others of both males and females.
b. In Form A, item 8c, please reconcile the models of the pilot studies for TNBS (is it ileitis or colitis).
c. In Form A, item 8f, please change the body condition score from 2 to <2.
d. In Form A, item 8g, please address the following:
    i. On the fifth page under intra-rectal administration, remove the re-dosing of anesthesia because the duration of the procedure is very short 30-seconds to a minute.
    ii. Under Longitudinal behavioral pain measurement, clarify whether the Von Frey and hotplate tests will be carried out for each experiment or if this is not the case indicate in which experiments and with what mice this will be done. If not addressed in this section then address it in the respective study tables in A,8,h.
e. In this section provide a specific description of how the OLFR78 mice will be handled in terms of the concentration of DSS and TNBS administration as prior work suggests this line is sensitive the respective agents.
f. In Form A, item 8h, please provide clarifications about the following issues:
    i. Clarify the terminal time point (7 or 8 days) for the LPA study with TNBS induced colitis and for the VIP study with TNBS induced colitis.
    ii. For the in vivo biotinylation studies with Angiotensin II and the NHERF1-3 Knockout Studies clarify how one can select a time point that shows the maximal effect if in all experiments the time points are only 7 or 7 and 42 days.
    iii. Clarify in vivo biotinylation studies what is meant by "shorter periods of time"; shorter than what?
    iv. Clarify how male and female mice will be distributed in experiments with genotypes that are indicated in item 4 as consisting of both sexes and clarify whether sex differences are expected or not and the basis for this expectation.
g. In Form A, item 13a, please add the information for the DSS and TNBS induced colitis models as they should be considered as having the potential to cause more than minimal pain and distress and delete the last several sentences under "Induction of TNBS ileitis" (In order to minimize ….13:377). Note this question asks the PI to list

all potentially painful/distressful procedures and justify, which also includes the DSS and TNBS rectal installation colitis models.

h. In Form A, item 13b, please re-do the literature searches with more targeted search terms, including colitis and ileitis models, and provide precise numbers of references identified.
i. In Form B, item 6c, surgery #1, please replace silk sutures with monofilament sutures for skin closure and reconcile the frequency of monitoring (2 times per day or every 6-8 hours).
j. In Form B, item 7, please change the body condition score from 2 to <2.
k. In Form B, item 9 should be completed specifically for the OLFR78 mice for the inducted colitis and ileitis models. For monitoring these animals should be monitored daily and, at a minimum, endpoint criteria should be severely hunched and or lethargic and a body condition score < 2 on a 5 scale. If weight will be assessed then indicate the freq. of the weight assessment and that 20% weight loss will also be an endpoint criterion.

19-159

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 4, it is not clear if animals will be purchased only or breeders purchased and then breeding at UIC. If breeding will be done at UIC, breeding form is required.
b. In Form A, item 7a uncheck chemical hazards and compounds listed as this is N/A.
c. In Form A, item 8a, please add one or two sentences summarizing what will be done to the animals in order to study/meet the objectives of this project.
d. In Form A, item 8f, clarify that mice will be monitored every day by animal care staff and every two days by research staff.
e. In Form A, item 8g, please address the following:
    i. Add the word "body" before "condition score <2" for humane endpoint criteria for all aims.
    ii. Under Aim 2, add the following words: "For transplant surgery, animals will be anesthetized with ketamine/xylazine and depth of ....."
    iii. Under Aim 3, verify that the humane endpoint of tumor size >5 mm diameter (312.5 mm^2 will allow to have sufficient time to determine tumor growth if the start of treatment will be when tumors are 200-300 mm^2. The humane endpoint in this aim appears to contradict the initiation timing for the project. Please note that ACC guidelines permit tumors to grow to 2 cm diameter. Please see item I,2 below for additional guidance on monitoring language.

iv. For all aims indicate how tumor size will be determined, i.e. will calipers be used and if so how animals are restrained for the measurement.

v. Please include size of needle for both intra-mammary pad and iv injection and indicate whether the mouse is anesthetized or manually restrained for IV injection.

vi. Describe the method of oral gavage including whether animals are manually restrained or sedated and that the gavage needle used is of appropriate size for mice and has a round ball at the end to minimize esophageal trauma. This is an item the DoD frequently asks.

f. In Form A, item 8h, verify that the requested numbers of mice per group will indeed allow 10-13 % reductions in tumor incidence and reconcile the numbers of mice for each genotype listed in this section with those listed in A4 and add the $Mcr4r^{-/-}$; $Foxn1^{-/-}$ and $Mcr4r^{+/+}$; $Foxn1^{-/-}$ mice here and indicate where in item 8.g. they will be used.

g. In Form A13b, please update search to include 2019.

h. In Form B, item 6a, please verify that the cross of $Mcr4r^{-/-}$ or $^{+/+}$; $Foxn1^{-/-}$ are nude or will have fur in which case shaving will be required.

i. In Form B, item 6c, please clarify monitoring until animals are awake.

j. In Form B, item 9, please address the following clarifications:

i. There are three different tumor models that need to be addressed for endpoint criteria. Aims 1 and 2 use the same endpoint criteria and the two models of naturally occurring and cell inoculation should be combined. Aim 3 mice need modified endpoint criteria as >5mm is less than the tumor size for initiation of the Aim 3 study.

ii. PI should indicate for the two sets of humane endpoint criteria the monitoring freq. for each, i.e. for Aims 1 and 2 monitoring is "Mice will be monitored every day by animal care staff and at least every two days by research staff" whereas for Aim 3 Mice will be monitored every day by animal care staff and at least every two days by research staff until tumors reach 200-300mm at which time research staff will monitor and measure tumor volume daily.

iii. Condition score <2 should be "body condition score <2"

19-164

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 8.g. (after page 13 of 26), please provide the following clarifications:

i. Add the words "of xylazine" after 2.2. mg/kg in the first line.

ii. Define the abbreviation LRS in the paragraph about Anesthesia.

iii. Remove the second sentence under Non survival training protocol (For the thoracic …. axilla), as no thoracic surgeries are described in B,6 or

add and thoracic procedures that might be conducted under this protocol.

iv. Reconcile the list of procedures at the bottom of the first page for general surgery/transplant training and urology/ObGyn training with what is in Form B, item 6. All surgeries listed in A,8,g should be described in B,6.

b. In Form A, item 14, please address the following:
   i. Personnel must update ACC Regulatory Training by updating online course "Animals and Research at UIC
   ii. Personnel must complete ACC Regulatory Training online course "Animals and Research at UIC":

c. In Form B, item 3 (page 1 of 14), please add i.v. LRS with anesthesia under fluid and electrolyte therapy.

19-139

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via a subcommittee of members 2 and 6 for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, correct the numbers here for the animals that were used and also reconcile with breeding form and review alignment.

b. In Form A, item 7d1., please check no box.

c. In Form A, item 7d2., please provide the method of sterilization of tribromoethanol (Avertin) and provide a justification for its use

d. In Form A, item 8g, please address the following
   i. Clarify in the table in the beginning of this item that the numbers initially required is the number justified in the statistical plan (~item 8.h) on the basis of power calculations and the number remaining required pertains to the number of mice that were not yet studied in the previous approval period in studies indicated as partly finished.
   ii. Reconcile the numbers of mice requested for each of the three aims with the number remaining required listed in the table.
   iii. Consider to change the ratio of the VDR+/+ and VDR-/- mice that will be co-housed in Aim 1 from 2:3 to 2:2, which will work better with the numbers of mice in each of the two experimental groups, i.e. there will be 5 cages of equal numbers of each strain.
   iv. Clarify why in aims 1, 2, and 3, animals will first be anesthetized for blood collection and then subjected to euthanasia by CO2 inhalation followed by cervical dislocation and why the animals cannot be cervically dislocated while anesthetized.
   v. Provide a rationale for using Avertin.
   vi. In Aim 2 remove the two sentences beginning with ER-positive and PR positive breast……." and ending with "…attaching to these receptors".
   vii. In Aim 3 change verb tense for groups to future tense.
   viii. In Aim 3 clarify why both groups 1 and 3 are needed. Could one control group serve as the control group for both the MCF& and MDA-MB-231 cells.

ix. In Aim 3 indicate if the mice are sedated or manually restrained for cell inoculation and the size of the needle used. PI also needs to clarify what is meant by experiments lasting over 3 weeks. What is the maximum time animals will be maintained and will humane endpoint criteria be used to determine the end of the study.

x. Under Monitoring and Humane Endpoint Criteria add the following words:
   1. Clarify that animals with ulcerative dermatitis will be euthanized.
   3. In line 7 of Aim 3 set 3: add the underlined words to the text "1.5 cm in diameter, we will …."

xi. Under Statistical Plan explicitly state that these numbers apply to those listed as the numbers initially required and not those remaining required and indicate the parameter that was used to calculate the effect size.

e. In Form A, item 10a, please change the second method from 2 to 5.
f. In Form A, item 10c, please uncheck the box.
g. In Form A, item 13.a., please remove all text and replace it with the requested information.
h. In Form A, item 14, please provide information about the duration of experience in the use of anesthesia and euthanasia for individuals #2 and #7 and their training if the experience has been only recent.
i. In Form B, item 3 "for other treatment" change verb tense to future.
j. In Form B, item 9, see comments above and reconcile.
k. In Breeding form, item 3c., please orrect the numbers.

9. Designated Review(s), Exemptions, and Lab Visits

a. Protocols

19-146

The Committee reviewed the protocol and discussed that the PI had addressed all veterinary comments and there were no additional clarifications needed and that when obtained the PI needed to provide the permits. Following discussion, a motion to approve this protocol with the following condition of initiation was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

b. Exemptions

Member 6 directed the Committee's attention to the following protocol requesting continuation of partial exemptions from the UIC Environmental Enrichment Plan this month. Following discussion that continuation of the partial exception was appropriate, a motion to approve continuation was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

18-203- The PI of this protocol has requested a partial exemption from the UIC Environmental Enrichment Plan. More specifically, the PI is requesting exemption from housing animals with social contact (both direct and indirect through mesh panels) following infection of animals with Mtb. The rationale behind the request is to prevent

spread of infection between animals and/or different study groups of animals. The exemption is only for the post-infection time period.

c. Lab Visits

Member 6 informed the Committee that the following labs were visited as part of the post-approval monitoring program.

[redacted]	17-155, 17-207
[redacted]	17-092, 18-099, 19-035
[redacted]	17-123, 18-132
[redacted]	18-107

10. New Business

a. Review of Guidelines/Policies

The Committee reviewed and discussed the editorial updates (version updates) to the policies/guidelines regarding euthanasia, RO bleeding, Tail snip rodents, Toe clipping rodent , Toe clipping for reptiles and amphibians and Zebrafish. Following discussion, a motion to approve this policies/guidelines was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

b. 19-174 Form H

The Committee reviewed the protocol and following discussion, a motion to approve this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

c. Modification of Protocol 18-039 Mod 5

The Committee reviewed the PI's request for addition of new strain of animals to conduct nerve injury studies at the level of the sciatic nerve instead of proximal portion of the tibial nerve. The Committee discussed that the PI needed to address the following: PI needed to verify the rat strain requested is the appropriate strain for the requested study, justify additional animals requested, clarify how animals are used in both models and indicate which animals will be maintained post injury and that the endpoint criteria and that post-operative care will be the same as in the original protocol, need to add details of nerve conduction studies, list painful procedure and conduct literature search. Following discussion, a motion that clarifications are needed to secure approval with designated member review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

d. Modification of Protocol 18-250 Mod 5

The Committee reviewed the PI's request for addition of 90 mice to existing nitroglycerin migraine and cortical spreading depression models to study neuronal branching and quantify dendritic cells using a AAV spaghetti monster vector. The Committee discussed that the PI needed to add the AAV spaghetti monster vector under non-pharmaceutical compounds and justify the use of it. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

e. Modification of Protocol 19-069 Mod 2

The Committee reviewed the PI's request to add chronic alcohol administration to the oncopig model system to further enhance the microenvironment of the pig's liver through induction of fibrosis for increasing live cancer take and maintenance. The Committee discussed that the PI needed to clarify the following: the duration of alcohol administration and duration of the study, who will be responsible for providing alcohol in water, how alcohol would be administered (water bottle, bowl, lixit, etc.), how will volume consumed be measured, how often the alcohol water is changed, and clarify if the alcohol diet is flavored, clarify if after 5 days of voluntary consumption if the pigs are placed solely on the 10% alcohol and water drinking solution, clarify if PI expects the pigs to develop signs of with drawl such as agitation, tremors, seizures during the 12-hour period in which animals will be taken off alcohol prior to an anesthesia event and finally . PI needs to indicate how animals are monitored during this time period should pigs be susceptible to alcohol withdrawal symptoms. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote:8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

f. Modification of Protocol 18-126 Mod 5

The Committee reviewed the PI's request for an additional 240 B6 mice to study a melanoma fibroblast lines modified with a Light R-B-Raf plasmid DNA to see if increased expression of B-raf in tumor and fibroblast cells with and without co implanted stromal cells can enhance tumor formation or promote tumor development. The Committee discussed that the PI needed to reconcile groups and number of animals between and the supporting tables and that PI needed to include age of animals, route of inoculation of cells, clarify if animals would be anesthetized, # and volume of cells, duration of study, freq. of monitoring with IVIS, a brief overview of IVIS procedure, reference to using the original protocol's endpoint criteria, how the light is turned on and off and how and when animals are euthanatized. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

g. Modification of Protocol 17-155 Mod 7

The Committee reviewed the PI's request for 20 additional animals to conduct a small pilot study with peptids. The Committee discussed that the PI needed to do the following: expand on the rational for the need to conduct a toxicity study, clarify the rational for requesting 2 animals/group, rational to use only males, need to provide more information regarding route, volume and frequency of administration of the test agent, need to indicate the duration of maintenance of animals post administration of test article, need to indicate if any biological samples such as blood will be collected and if so indicate the method of collection, need to include description of monitoring program and endpoint criteria post-test article administration and need to conduct literature search. Following discussion a motion to defer this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

h. Modification of Protocol 18-077 Mod 3

The Committee reviewed the PI's request to add stereotaxic injection to further the understanding of mechanisms associated with chronic pain and opioid drug. The Committee discussed that the PI needed to do the following: needed to provide more specific information on how this surgical technique fit into the context of the original protocol and the studies/models approved in the original protocol, need to clarify who will perform the surgery and their level of experience with this kind of surgery and need to correct the analgesic dose and timing. Following discussion a motion to defer this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

i. Modification of Protocol 17-125 Mod 13

The Committee reviewed the PI's request to add stereotaxic injection of an agents and two nerve injury models to further the understanding of mechanisms associated with chronic pain and opioid drug administration. The Committee discussed that the PI needed to do the following: need to provide more specific information on how this surgical technique and nerve injury models fit into the context of the original protocol and the studies/models approved in the original protocol, provide humane endpoint criteria, need to clarify who will perform the surgery and their level of experience with this kind of surgery and need to correct the analgesic dose and timing. Following discussion a motion to defer this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

j. Modification of Protocol 19-044 Mod 01

The Committee reviewed the PI's request to add OCT imaging procedure as a method of assessing retina microvascular changes that could be an early indicator of Alzheimer's disease. The Committee discussed that the requested procedure will last approximately 30 minutes and the animals will be under anesthesia, and that PI is currently using MRI. The committee discussed that PI needed to provide the following detail: need to clarify if

additional animals or different strain of animals needed and also if animals will undergo also undergo MRI in addition to OCT and needed to provide more details on the study design as it pertains to how OCT will be incorporated into the current study, including number of OCT procedures, time between OCT procedures and approx., age of animals at time of OCT procedure and when animals will be euthanatized. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

k. Modification of Protocol 17-077 Mod 06

The Committee reviewed the PI's request for additional 630 mice to test a new series of compounds in the PI's ocular HSV-1 mouse model. The committee discussed that PI needed to do the following; need to clarify which mouse strain will be used for these studies, rationale behind the total number of mice requested, need to clarify if ocular scoring and viral shedding detection, etc. is the same as originally approved in the original protocol, need to clarify if all tests are conducted weekly and at the same time, which tests require anesthesia and what the anesthesia is, and the location and need to clarify if aseptic technique will be used for reconstitution of drugs. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via subcommittee of members 6 and 10 for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

l. Modification of Protocol 18-079 Mod 02

The Committee reviewed the PI's request for additional 460 mice to test a new series of compounds in the PI's genital HSV-2 mouse model. The committee discussed that PI needed to do the following; need to clarify if only female mice will be used for studies, need to clarify the timing of prophylactic and therapeutic treatment, need to clarify and justify the group sizes, need to clarify HSV-2 genital infection, viral shedding and detection is the same as originally approved in the original protocol, need to clarify if aseptic technique will be used for reconstitution of drugs and need to clarify if ACV and IZV are pharmaceutical grade. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via subcommittee of members 6 and 10 for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

m. Modification of Protocol 18-050 Mod 04

The Committee reviewed the PI's request to add pain behavior studies with addition of 32 each of UAB knock in model (B6;129-Hbatm1(HBA)Tow Hbbtm2(HBG1,HBB*)Tow/J (genotype S/S)) to determine if reduced levels of selenium in diet affect SCD (sickle cell) pathology in the HbSS mouse model. Also the committee discussed PI's request to transfer animals from one facility to another facility for purpose of behavioral testing.

The committee discussed that PI needed to do the following; need to notify the vet staff prior to initiation of this project in regards to logistics of the study, need to clarify if equal number of males and females will be used for study, need to clarify when behavioral evaluations will be done and will all animals go through all the tests and the frequency of the tests (except for the frequency for conditional place preference that has been and that PI needed to check the group size and number of group against number of additional animals requested and correct accordingly. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

n. Modification of Protocol 17-208 Mod 01

The Committee reviewed the PI's request to study the role of FoxM1 in Leukemia, request for addition of new strain of mice: 60 FoxM1 fl/fl; mx-Cre tg c57, addition of funding and addition of new personnel. The committee discussed that PI needed to do the following; need to provide a study design table to clearly outline the groups and treatments and donor/recipient animals, need to indicate the volume of 5-FU that will be will be administered to animals, need to provide the volume for compound and control treatment and treatment duration, need to clarify the timing of the treatment in relation to the Plpc treatment and duration of treatment, need to provide the volume that would be injected retro-orbital, need to verify that endpoint criteria used is the same as what is approved in the original protocol, need to add PlpC and 5_FU to non-pharmaceutical compound table the table and to indicate for all three agents how they are sterilized prior to use and need to provide Breeding form for breeding and generation of Mx-Cre Foxm1fl/fl. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

o. Modification of Protocol 18-111 Mod 04

The Committee reviewed PI's request for addition of 16 pregnant females to generate primary mixed glial cell cultures, to study the effects of 3 drugs (LKE, RK101 and S-LCM) to no treatment on OPC viability and maturation and also 30 new LKE derivations and 6 RK101 for testing (these already been tested for toxicity and higher efficacy). The committee discussed that PI needed to make a minor correction. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

p. Modification of Protocol 17-060 Mod 47

The Committee reviewed PI's request to place animals in restrainer for up to 120 minutes for purpose of consecutive test article delivery. The committee discussed that PI needed to do the following: that PI needed to provide description of the restrainer and a picture of the device, need to describe the acclimation process of animals to the restraint device, need to describe the monitoring program for animals maintained in the restraint device for the two hour restraint period and to describe endpoints for temporarily or permanently removing an animal from the restraint device. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this modification was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

ANIMAL CARE COMMITTEE BMEETING MINUTES
NOVEMBER 19, 2019

Attendees: Member 2, Member 6 (*arrived late*), Member 8, Member 9, Member 10, Member 11, Member 24 (*left early*), and Member 30

Absent: None

Guest: Member 40

1. **Minutes**

Minutes were sent for designated review determination.

2. **Announcements**

There were no announcements.

3. **Old Business**

a. Modification of Protocol 18-162 (03)

The Committee reviewed the PI's request for 5 additional animals to increase group size for two groups. The Committee discussed the following: in explanation, remove all references to remaining animals, and remove last 3 paragraphs, in table remove groups that were not completed, in 5b, insert time line, clarify specific groups animals will be added to and provide justification for any differences between previous animals and new animals, and indicate specific parameter to be assessed and justify group size with power analysis, and that PI needs to meet with members 2 and 6 prior to submitting revisions. Following discussion, a motion that revisions were to be sent for designated member review determination to the Committee was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions and 0 recusals.

b. Modifications of Protocols 17-125 (13) and 18-077 (03)

The Committee reviewed the PI's request for addition of surgery for stereotaxic injections (both) and addition of animals for two new models (17-125). The Committee discussed that the PI needed to address the following: that compound proposed was toxic and use in rodents at dose proposed must be provided, that the title was incorrect, that numbers were incorrect, that the two new models were not appropriately justified, that the abbreviations needed to be defined, how treatment centrally is tied to the new models, remove SCD mice as this is covered under another protocol, rewrite the description to clarify the two models and the separate groups needed for each and whether separate groups would be needed for each brain region, that a clear time line for all test before and after surgery was needed, and how the half-life of compound would affect timing for testing and how effects that were not from surgery would be determined, rewrite the surgical description to clarify when analgesic was administered, the order in which

procedures are conducted, coordinates for injection, skin dissection, and expertise with the procedures, clarify sterilization of instruments, and monitoring post-operatively. Following discussion, a motion that significant clarifications were needed prior to rereview and to defer this modification was passed by the following vote:

c. Modification of Protocol 17-155 (07)

The Committee reviewed the PI's request for additional animals to determine maximum tolerated dose of compound. The Committee discussed that the PI needed to clarify purpose for this protocol, the group numbers to be included and the total number to be included, clarify if MTD would be defined as NOAEL or if mild/moderate AEs would be acceptable, indicate location for doing and isoflurane scavenging, the interval beginning doses, indicate the weighing would be daily, indicate method of euthanasia for this study, and remove single housing. Following discussion a motion that clarifications are needed to secure approval with designated member review following full committee review via subcommittee of members 2 and 6 was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

d. Protocol 17-175 Update

The Committee discussed that the trainers in the laboratory had been retrained on euthanasia procedure using CO2 and secondary method by members of the veterinary staff.

4. [redacted] Director's Update Legislative and Facility Update

The Committee discussed the following: 1) that the annual USDA animal usage data was being complied and the goal was to submit by November 22nd, 2) that a PO had been issued to purchase a dry heat bulk sterilizer with installation schedule to begin in March, 3) that the project to replace and upgrade the HVAC system in the [redacted] was ongoing, and 4) that [redacted] was getting ready for reoccupation and that the facility had been sanitized and sentinel animals had been moved into the facility to monitor for the presence of murine pathogens.

5. [redacted] Update

a. Modification

Member 2 updated the Committee to the following activity during the past month: there was 1 modification approved via administrative level, 45 modifications approved administratively following veterinary consult, and 4 modifications approved via designated review this month. In addition, there were 46 protocols that added personnel,

0 with personnel deletions, 0 with addition of funding, and 0 addition to the holding protocol.

b. Continuations and Terminations

Member 2 directed the Committee's attention to the protocols for continuation and those terminated due to expiration or PI's request. The Committee discussed that all protocols had completed the appropriate continuation documents and a motion for designated member review for renewal the protocols was passed by the following vote: 7 in favor, 0 opposed, 0 abstention, and 0 recusals.

6. Review from Subcommittee #1

19-168

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, correct use type and reconcile numbers
b. In Form A, item 5c, line 2, correct room to 212.
c. In Form A, item 7d2, please clarify if first drug is SAHA.
d. In Form A, item 8e, please address the following:
    i. Indicate that C57 will be used as a control for C57 strains. Remove reference to background strain for BTBR.
    ii. Under BTBR, remove reference to C57 background.
e. In Form A, item 8f, remove answer as this is N/A to this study.
f. In Form A, item 8g, please address the following:
    i. Under PNS, add that pregnant C57 mice will be obtained from vendor.
    ii. Under Brain perfusion, change 5% isoflurane to ketamine/xylazine (100/25 mg/kg IP).
    iii. Under study 1a, correct total numbers
    iv. Remove "For chronic ethanol…of age)."
    v. Under Study 2, please address the following:
        1. Please clarify which behavior tests will be conducted and provide description as to how grooming behavior will be assessed.
        2. Remove + saline as there are no drug treatments and clarify why X2 is indicated. Based on study, only 10 mice per strain should be requested.
    vi. Table of studies, correct numbers for study 2, remove study 3, remove BTBR mice as these were accounted for on line 1 and reconcile totals and with A4.
g. In Form A, item 10a, correct biochemical study euthanasia to #1, remove anesthetic and list inhalation as this is method described in A8g.

h. In Form A, item 10c, uncheck boxes.
i. In Form A, item 13b, please clarify use of schizophrenia as part of search.
j. In Form A, item 14, remove personnel #2 as there are no rat studies.
k. In Form B, item 3, add oral gavage.

19-169

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, numbers need to be revised based on whether there is a normoxic group for each and dams are rotated.
b. In Form A, item 5c, please list fundus imaging and angiography and indicate location.
c. In Form A, item 7c, check 'no'.
d. In Form A, item 8g; Please address the following:
    i. Under OIR model, please address the following:
        1. Please clarify whose hyperoxia chambers will be used for this study and who will train personnel on the use of the chambers.
        2. Line 2-3, please clarify that pups with dams will be exposed to 75% hyperoxic conditions from PN day -12 or to normoxic conditions and that dams will be rotated between normoxic and hyperoxic conditions every 24 hours (for revised strategy).
        3. Remove the line "no health issues in the adult nursing mothers exposed to 5 days of 75% O_2 has been observed".
        4. Clarify that on PN day 17, dams will be euthanized and how.
        5. Please indicate that protocol staff will receive training from veterinary staff on SOPs for working in hyperoxia room prior to initiation of this project.
    ii. Under Intravitreal injections, please address the following:
        1. Change untreated to normoxic in line 1.
        2. State the concentrations of exosomes that will be injected.
    iii. Under 'fundus photography and fluorescein angiography', please change the dose for ketamine and xylazine to 100mg/kg and 5 mg/kg respectively
e. In Form A, item 8h, please address the following:
    i. If dams are rotated for each group then numbers in table need to reflect normoxic controls. If not, please correct the number of pups accordingly.
f. In Form A, item 13b, include a search for oxygen-induced retinopathy, and exosomes.
g. In Form A, item 14, update training dates ACC regulatory date for PI.
h. In Form B, item 6d and 6e4, please uncheck the boxes as no surgery is involved.
i. In Form B, item 7, please provide description and monitoring frequency for intravitreal injections.
j. Breeding form, please address the following:

i. Item 1, remove last line. See comments above.
ii. Breeding #1, please correct as follows:
    1. Correct average # of litters/female to 1 as females should not be reused after hyperoxia exposure.
    2. Reconcile numbers if there will be matched normoxic controls.

19-180

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2b, please check the box 'other project staff' for personnel
b. In Form A, item 7c, please include [redacted].
c. In Form A, item 8b, Please define the abbreviations TNBC and ECs and remove the paragraph describing study design. This is not required in this section.
d. In Form A, item 8g, Please address the following:
    i. Remove re-administration of isoflurane every 15 minutes for hair removal.
    ii. Matrigel (proposed for dilution of tumor cells) should be included in section 7b
    iii. Please remove reference to who will inject tumor cells and trainer experience this is not required in this section
    iv. If Non tumor implanted mammary fat pad tissue from the treated mice will serve as control- please justify the use of RiboTag$^{fl/fl}$ mice.
    v. Under experimental procedures, in the paragraph describing the humane endpoints: in #1, change the % body weight from 10% to 15% and remove #6 referring to abdominal girth.
    vi. Please change "cell lines" to cell line as there is just one cell line (P8119) that will be used in the experiments designed in this protocol.
e. In Form A, item 8h, When one sample (obtained by pooling tissue from 4 mice) is sufficient for both RNA seq and qPCR analysis then justify the requirement of 30 mice each for RNA seq and qPCR.
f. In Form B, item 9; change the % body weight from 10% to 15% and remove #6 referring to abdominal girth.

19-187

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, items 5a and 5c, please clarify why both [redacted] and [redacted] are listed as PI has conducted all previous work in [redacted]. [redacted] should be removed, or in A8g, specifically state which studies will be conducted in [redacted].
b. In Form A, item 5c, list [redacted] and IVIS.
c. In Form A, item 7b, check "Yes" and provide requested information for use of Matrigel for SQ cell suspension preparation.
d. In Form A, item 7c, please see comment above related to location and reconcile.
e. In Form A, item 8f, PI should check "NO" and remove answer, as nude and SCIDs do not need to be listed here.
f. In Form A, item 8g, please address the following:
    i. Please verify that SC injections are unilateral for each study.
    ii. Indicate experimental time line and study duration for each experiment.
    iii. Indicate volume of injection for BrdU and route of administration for D-luciferin.
    iv. Clarify when IVIS imaging will be conducted.
    v. See comments above related to location and reconcile.
    vi. For IC studies, remove current end points as most do not apply to this tumor route. Respiratory distress, jaundice, 15% weight gain, severe abdominal distension, and BSC <2 should be used. In addition, clarify the frequency of monitoring.
g. In Form A, item 8h, include tabulated treatment groups for each experiment and reconcile the total number with A4.
h. In Form A, item 10a, specify that the route of administration is by inhalation in column 4.
i. In Form A, item 12, check "Yes" for surgical castration
j. In Form A, item 14, please address the following:
    i. Indicate personnel that will be responsible for experimental diet feeding.
    ii. Indicate personnel that will be performing intracardial injection and their expertise with the procedure. If none, then indicate that personnel will receive training from veterinary staff prior to initiation.
    iii. Indicate personnel that will be performing castration and indicate that training will be received from veterinary staff and remove collaborator from protocol as the trainer.
    iv. Personnel need to update online training.
k. In Form B, item 4, correct dose of xylazine to 10 mg/kg.
l. In Form B, item 6a, remove "tamed iodine" and indicate that betadine or chlorhexidine scrubs will be used for sterilization of surgical site.
m. In Form B, item 6b, correct dose of ketamine/xylazine to 100/10 mg/kg.
n. In Form B, item 6c, please address the following:
    i. Line 5, specifically state that ligation of the right and left spermatic cords is performed separately.
    ii. Line 6, indicate the incision is closed in two layers- tunica is closed with PDS and skin is closed with either nylon suture or wound clips. .
o. In Form B, item 6e, check box to acknowledge requirements for post-operative monitoring.

p. In Form B, item 9, please address the following:
    i. For SC tumors, please replace humane endpoint criteria with language used in A8g and indicate the frequency of monitoring.
    ii. For IC tumors, please clarify the frequency of monitoring once tumors are detected. Is this 3 times per week?. In addition, see comments above and reconcile here for humane endpoint criteria

Member 6 arrived

19-170

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, please address the following:
    i. See comments below about consolidation of experiments and correct numbers here.
    ii. For Rag mice correct the total to match A8g.
b. In Form A, item 8g, please address the following;
    i. Prior to study descriptions, clarify that veterinary staff will be contacted several months prior to the study of hMISTRG studies to discuss logistics and health status of the animals. Animals will be ordered through unapproved vendor site.
    ii. It appears that some of the studies are redundant and should be removed. Please review and remove the redundant studies and reconcilw numbers with A4.
    iii. Expt 20, please address the following:
        1. Please indicate that anticipated tumor kinetics for the SC tumors and when it is anticipated that tumors would reach 2 cm or begin to ulcerate and require tumor resection. Based on the proposed study design the whole study is 28 days- up to 14 days or initial priming and then 14 days post intra-splenic administration.
        2. Please clarify that animals will not undergo SC tumor excision if they have body condition score <2 and that these mice will be euthanized. It needs to be clear if SC tumor excision is during the same surgical setting as laparotomy for intrasplenic injection or conducted as two surgeries. It appears from B6c, that this may be two surgeries.
c. In Form A, assurance must be signed by PI.
d. In Form B, item 5a and 5b, account for two surgeries for expt #20.
e. In Form B, item 6c, please list second surgery to describe direct heptic tumor inoculation or direct hepatic PV inoculation. It should be clear in the case of direct hepatic PV that this is a second surgery.
f. In Form B, item 9, remove reference to A categories from this protocol.

19-182

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via subcommittee of members 2, 6, and 10 for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 4, only list experimental numbers and reconcile numbers with A8g/h. Ensure that all strains are included in this table.
b. In Form A, item 5c, please address the following:
    i. Line 1, remove LPS and HDM from line 1 to line 2.
    ii. Line 2, add LPS and HDM here and list [redacted]
    iii. Define HDM here.
    iv. Line 5, remove [redacted]. These mice will be maintained in [redacted].
c. In Form A, item 7b, uncheck yes and check no and remove BrdU as this is not a murine biologic.
d. In Form A, item 7c, please list the following rooms [redacted] and [redacted] and indicate active charcoal scavenging.
e. In Form A, item 7d2, BrdU should be included here.
f. In Form A, item 8a, please revise this section so that it is written in more lay terminology.
g. In Form A, item 8d, this must focus on why animals are required and not specifically mice. Most of this information should be moved to A8e as an introduction prior to strain justification.
h. In Form A, item 8e, please remove maintenance of CX3CR1CreER:R26Tomato:Csf1R fl/fl under this protocol. This should be done PI's other protocol.
i. In Form A, item 8g, please address the following:
    i. In overview paragraph, please address the following:
        1. Please indicate that all mice will be breed under PI's other protocol and experimental mice will be transferred to this protocol.
        2. Please clarify if the pairs are cohoused together prior to surgery to ensure they are compatible and do not show aggression toward each other and that animals that do show aggression will not be used for surgery.
        3. Please clarify the what will happen to animals that show aggression post-surgery. What level of aggression will warrant removal from study and euthanasia?
        4. Please indicate that prior to initiation, PI will inform veterinary staff so that veterinary staff can observe initial surgeries.
    ii. For any procedure involving injections, add induction with isoflurane followed by ketamine/xylazine for pairs.
    iii. Under procedure #1, please remove frequency of blood sampling from this section and include under individual experiments as time points differ between studies.

iv. Under procedure #3, please indicate CO2 followed by cervical dislocation for euthanasia.
v. Under procedure #4, please address the following:
    1. Change infectious to inflammatory in the title.
    2. Please clarify that each mouse in the pair is anesthetized.
    3. Please clarify which of the two animals will have agent administered. Is it the non-reporter animal?
vi. Under procedure #6, please clarify that after day 3 if animals are stable, they will be monitored twice per week until the end of the study.
vii. Under procedure #7, please indicate monitoring to 4 times daily for first 3 days and then if the animal is stable a minimum of twice daily observations until the end of the study and indicate that same humane endpoints as outline in procedure #6 will be used.
viii. Under procedure #8, please indicate that that same humane endpoints as outline in procedure #6 will be used.
ix. Under procedure #9, please clarify that animals will be monitored once daily for first week and then twice weekly thereafter if animals are stable and that same humane endpoints as outline in procedure #6 will be used.

j. In Form A, item 8h, please address the following:
    i. For all procedures that will involve anesthesia, it is recommended that PI use isoflurane induction and then injection IP with ketamine/xylazine.
    ii. Study 1, change # of mice to # of pairs in table 1 and 2.
    iii. Study 2C, please address the following:
        1. Reconcile text above table with time points below table. Text only indicates two weeks, but there are 3 time points.
        2. Please correct blood sampling frequency as this is once per week and not 3 times per week and please clarify maximum blood collection volume.
    iv. Study 2D, please address the following:
        1. Reconcile text above table with time points below table. Text only indicates two weeks, but there are 2 time points and the maximum is 7 days.
        2. Please correct blood sampling frequency as this is once per week and not 3 times per week and some time points are prior to the time points listed and clarify maximum volume.
    v. Study 2E, please clarify maximum blood collection volume.
    vi. Study 2F, change table # to 6 and clarify blood sampling frequency and times points.
    vii. Table 3-5, column 2, change to No. pairs/group.
k. In Form A, item 13a, please clarify whether or not there are reporter mice that could be crossed that would allow distinguishing the contribution of circulating monocytes and monocyte-derived macrophages in the presence of embryonic-derived macrophages and if so, then answer A13c also.
l. In Form A, item 14, please specifically include surgery as a procedure for personnel and clarify for personnel #2, that PI will be training on surgery.
m. In Form B, item 6c, please address the following:
    i. Surgery 2, line 2, correct to buprenorphine SR LAB.

ii. Surgery 3, BAL terminal surgery must be described here.

n. In Form B, item 7, please address the following:
   i. Line 3, correct to buprenorphine SR LAB and clarify if this is a second dose of analgesia as the first dose is given at the time of surgery.
   ii. Please indicate that animals will be anesthetized for wound clip removal via induction with isoflurane followed by ketamine/xylazine (100/5mg/kg IP).

o. In Form B, item 9, please correct monitoring criteria and humane endpoints to match what is requested for A8g.

7. Review from Subcommittee #3

19-181

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2b, please provide a work phone number for first personnel listed in this section.
b. In Form A, item 7a, please provide an IBC approval number and list bacterial agent. IBC must be approved for transfection of this specific bacterial agent with the genes listed.
c. In Form A, item 7d2, please list bacterial agents here and include preparation of reagent for administration. Include the specific source of the parent strain.
d. In Form A, item 8b, please provide reference to use of this specific strain used for IV administration and what specific products this strain is used in for human health.
e. In Form A, item 8g, please address the following:
   i. Prior to description of procedures and experiments, indicate that prior to ordering animals for this protocol, veterinary staff will be informed of when the study will be initiated.
   ii. Under local SC injection, please address the following:
      1. In paragraph #3, please add the following to the last sentence: "…or until animals reach humane endpoint criteria as indicated below".
      2. In paragraph 4, indicate the specific vein in which bacteria will be injected and indicate if chemical restraint (anesthesia) or physical restraint with restraint device or manually will be used and provide details.
   iii. Under experiment #1, please address the following:
      1. In the paragraph under group listing, please reverse the order of the last two sentences to list method of euthanasia first prior to the description of necropsy.
      2. Under humane endpoints, delete "abnormal…physical".

iv. Under experiment #2, humane endpoints, , delete "abnormal…physical".

f. Delete the entire paragraph labeled H.

g. In Form A, item 8h, please address the following:
   i. Correct the section labeled 2. Justify the use of animals…, to A8h.
   ii. Clarify why only male animals are proposed for experiment 2.
   iii. All text up to "For xenograft experiment" should be deleted.
   iv. Indicate what the unit of the differences in Table 2. Is this mm3 or something else?

h. In Form A, item 9, please check contact PI and contact other.

i. In Form B, item 3, please indicate in which vein the bacteria will be injected and check the yes if anesthesia will be used for this purpose.

j. In Form B, item 9, please address the following:
   i. Change the tumor size from 50 mm to 50 mm^3.
   ii. Delete "abnormal…physical" on lines 4-5.

19-183

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review via subcommittee of members 2 and 6 for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 7b., please note that PDX tumor lines from sources outside UIC must be screened for excluded murine agents.

b. In Form A, item 8b, please address the use of PP versus PPP formulations of CNP in the scientific background section.

c. In Form A, item 8c, please clarify if there were any publications from this research in the last 3 years.

d. In Form A, item 8g, please address the following:
   i. Under Aim 1.3, Procedure, please address the following:
      1. In the second paragraph, please address the following:
         a. In the first sentence, please clarify that mice will be injected with one of four tumor lines as shown in the table below.
         b. The formula used yields tumor volume, not the stated tumor weight. Please correct.
   ii. In third paragraph, please address the following:
      a. Please rewrite the first sentence to the following: "…bearing Herceptin sensitive, Herceptin resistant, Lapatinib resistant, or Hepceptin/Labatinib resistant will be…".
   iii. The last two sentences of paragraph 3, do not agree with the numbers above the table or with the table and need to be reconcile. If there are 3 groups of compounds (empty, PP-CNP, and PPP-CNP) X 2 routes X 3 mice/route X 4 cell lines this equals 72 mice for route determination. Once route is determine what is the total per group? Is this 7? If so 7 X 1

route X 3 compounds X 4 lines = 84. This would be a total of 156 and not 208. Please reconcile all sections regarding this issue.

iv. In paragraph 4, please add body score of <2 as criterion, change the tumor size from "2 cubic cm diameter" to "2 cm diameter", and indicate that the animals will be euthanized by opening of the chest followed by exsanguination.

v. In the table for Aim 3.2, move mention of the 5 mice for validation to a footnote to this table.

e. In Form A, item 8h, please provide clarifications about the following issues:
   i. For Aim 1.3, reconcile 10 animals for Aim 1.3 with the number of 13 animal per group current listed in A8g table and with the comments above.
   ii. Please correct statistical
   iii. In aim 3.1 add the 33% extra animals needed for the Herceptin resistant group.

f. In Form A, item 13b, please clarify search for alternatives as the number of references is not correct..

g. In Form A, item 14, personnel need to update ACC Regulatory training and training dates.

h. In Form B, items 4 and 6e, please clarify whether meloxicam will be used and if so, it should be added in item 4 and it should be clarified in B6c when it will be used instead of buprenorphine.

i. In Form B, item 6c, surgery #1, please address the following:
   i. Please clarify mammary fat pad clearing.
   ii. Please indicate what type of monofilament suture will be used and when sutures or clips will be removed.
   iii. See comment above related to buprenorphine or meloxicam and reconcile.

j. In Form B, item 9, please address the following:
   i. Add the frequency of measuring tumor size.
   ii. Reconcile humane endpoints with corrections requested for A8g.

k. In Breeding form, numbers need to be corrected and reconciled with A4 and A8g/h. , please address the following:

19-184

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 7a, please provide a current IBC approval number for this specific project.

b. In Form A, item 7d2, please address the following:
   i. For all compounds listed, please correct the degree symbol.

ii. Starting with PBS down to Ascorbic acid, the last column is incorrect and should be moved to the line below and a description of how PBS is prepared needs to be provided.
iii. It is also not clear from A8g and A8h when and how ascorbic acid and chitosan are administered. Either remove from this table or clarify in A8g/A8h how when and how these are administered. If they are part of a formulation with other agents listed here, then the preparation of those agents must be modified to clarify this issue.

c. In Form A, item 8c, please indicate that this protocol was not initiated in the past three years.
d. In Form A, item 8g, please address the following:
    i. Add a time line for the experiments.
    ii. Under A) indicate when after BCG injection treatment is initiated.
    iii. Under C),please address the following:
        1. Provide the information for dose, volume, frequency, and route of administration of each treatment. It is suggested that a table be provided. ;
        2. Indicate the size of the needle used for the IP injections.
    iv. Under D) indicate that the retro-orbital blood sampling will alternate eyes between samples.
    v. Under F), clarify the 5th week indicates the 5th week after BCG or the start of the nanoparticle treatment.
    vi. Below item F, add a description of the humane endpoints that will be used to determine premature euthanasia, including problems such as draining tracts and infection of injection sites.
e. In Form A, item 8h, please address the following:
    i. Please clarify the specific request for training animals.
    ii. PI should consider the effect of the multiple comparisons on the statistical analysis.
f. In Form A, item 14, please indicate protocol staff's experience with oral gavage. Protocol staff will need to demonstrate proficiency with oral gavage in mice to veterinary staff prior to initiation.
g. In Form B, item 3, please clarify the substances that will be injected and gavaged and check the yes or no boxes for gastric gavage and i.p. injections
h. In Form B, item 4, please delete mention of fentanyl.

19-185

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 2b, please provide emergency (non-UIC) phone numbers for personnel listed in here.
b. In Form A, item 8g, please address the following:

i. Clarify in the first sentence who this training will serve. The training will probably serve more people than just the investigator as now currently indicated, so indicate who the surgical trainees are. Are these residents, fellow, community physicians?
ii. Indicate the concentration of the phenylephrine and tropicamide.
iii. Under the 6th bullet point, clarify what is meant by "free of insertion".
iv. Add as last bullet point Euthanasia and indicate method.

c. In Form A, item 13a, please remove the first 2 sentences as they are not relevant to the use of swine and correct the second to last sentence to read ".....train physicians before they perform the procedures on humans."
d. In Form A, item 14, personnel need to update ACC Regulatory training.
e. In Form B, item B6c, please include all details in this section.

Member 24 left

8. Review from Subcommittee #2

19-173

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals.

a. In Form A, item 7c1, please indicate the location as 7369 JBVMC.
b. In Form A, item 8a, please rewrite the section in lay terms and include bupivacaine toxicity and its clinical relevance to the goal this project.
c. In Form A, item 8b, this section indicates that a range of bupivacaine doses will be tested, but in A8g, only one dose is being tested. Please reconcile.
d. In Form A, item 8d, please indicate that computer models or in-vitro models are not alternatives to animal model for this project.
e. In Form A, item 8e, first paragraph, please remove the 2nd sentence.
f. In Form A, item 8g, please address the following:
    i. The lipid emulsions dose in text indicates a range (3-5 ml/kg for bolus and 0.6-1.0 ml/kg/min for infusion), but in table 1, different doses are indicated. Please reconcile the doses.
    ii. Please remove figure 1 and the foot notes. These are not a representative of the study in this protocol.
    iii. Please include a section on resuscitation of animals including the method (chest compression), the duration resuscitation will be attempted, and the timing. In addition, indicate what happens when the animals is revived. Will animals be placed back on anesthesia?
    iv. For intubation, please include that this may also be via surgical method (tracheostomy) that is described in Form B as well as via oral route for intubation.

g. In Form A, item 8h, please address the following:
    i. Justify why only male animals are used.
    ii. In this section, a range of bupivacaine doses is indicated, but in A8g only one dose is being tested. Please reconcile.
    iii. Please delete statement about confirmation studies.
    iv. Please correct the doses of lipid doses in the table.
h. In Form A, item 10a, line 1, column #2, remove answer and list method 2 and column #3, verify that the dosage indicated for the dose of sevoflurane is correct.
i. In Form A, item 12b, Mark "Yes" for surgery
j. In Form A, item 13a, justify the surgical procedure, chest compressions and also LAST.
k. In Form A, item 13b, please indicate the actual terms used for literature search and also conduct a search for surgical procedure.
l. In Form A, item 14, for personnel #1, please indicate the date for ACC training as 8/6/18.
m. In Form B, item 3, remove answer as this is part of the terminal surgery.

19-176

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 3a, please correct funding source.
b. In Form A, item 5a, uncheck "[redacted]".
c. In Form A, item 7d1, check "No".
d. In Form A, item 7d2, please add the magnetic beads to the table and provide the required information.
e. In Form A, item8c, please remove your answer.
f. In Form A, item 8g, please address the following:
    i. Under technical overview, remove cell line development from section 2 title and remove first 7 lines. This is not required.
    ii. Please verify if injection needs to be repeated that it is in the same limb as the initial injection, the maximum duration animals are observed for tumor growth prior to reinjection, and the maximum number of re-injections that a single animal will receive for tumor growth in hindlimb.
    iii. Under Liver tumor Implantation, define TACE.
    iv. Please clarify the treatment for control animals.
g. In Form A, item 8h, line 1, please remove the word "additional".
h. In Form A, item 13b, please conduct search for alternatives for laparotomy procedure.
i. In Form A, item 13c, as no alternatives were found, remove this answer.
j. In Form A, item 15, signatures are required.
k. In Form B, item 3, please add hindlimb injection under "other treatment" and check "Yes" for use of anesthetic.

l. In Form B, item 4, please remove dexmedetomide and replace with xylazine at 5 mg/kg.
m. In Form B, item 6c, please address the following concerns:
    i. For both surgeries, replace dexmedetomide with xylazine at 5 mg/kg.
    ii. For Surgery 2 - dose for ketamine should be 45 mg/kg and not 30 mg/kg.
n. In Form B, item 7f, this section needs to be answered.

19-177

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed prior to rereview by full committee review and to defer this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 8b, please address the following:
    i. Based on reference sited and text in this section, this model has only show histological signs, but no behavioral signs. The Committee suggests staging with step #1 is model development and step #2 is treatment and the PI. In addition, clarify the previous study versus this one and that PI will update ACC for model.
    ii. Please clarify what this model is trying to replicate. This section mentions MSA-P, MSA-C, and a mixed pathology. Which of these is the AAV-OligOO1-alpha synclein trying to mimic?
b. In Form A, item 13b, please update the search to conduct a broader search.
c. In Form B, item 6f2, please replace Simbadol with Buprenorphine SR 0.2 mg/kg SC.

9. Designated Review(s), Exemptions, and Lab Visits

a. Protocols

19-175

The Committee reviewed the protocol and discussed that PI had addressed clarifications based on prereivew and there were no additional clarifications needed. Following discussion, a motion to approve this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

19-178

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for

this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form A, item 8h, provide the power analysis used to determine 9 mice per group

b. Exemptions

Member 6 indicated that there was one protocol requesting continuation of partial exemptions from the UIC Environmental Enrichment Plan this month. The Committee reviewed the request and a motion to approve continuation of the request was passed by the following vote: 8 in favor, 0 opposed, 0 abstentions, and 0 recusals

18-222- The PI has requested a partial exemption from the UIC Environmental Enrichment Plan. More specifically, the PI is requesting exemption from pair housing during toxicity, efficacy and/or PK studies to facilitate animal observations such as clinical assessment for vomit and diarrhea, and food consumption. Animals can be pair housed prior to and following study and they can have mesh contact with other animals during the study.

c. Lab Visits

Member 6 directed the Committee's attention to the laboratories that were visited as part of the post-approval monitoring program.

[redacted]	17-190, 18-039, 18-156
[redacted]	17-219
[redacted]	17-025
[redacted]	18-013
[redacted]	17-044
[redacted]	18-104
[redacted]	16-201, 18-117
[redacted]	17-058, 18-199, 19-120
[redacted]	17-093, 18-038

10. New Business

a. Semiannual Programmatic and Inspection Reviews

Member 2 directed the Committee's attention to the Programmatic Review Report. The Committee noted that there were no deficiencies noted. Member 2 directed the Committee's attention to the veterinary review and no deficiencies were noted. The Committee reviewed and approved the report of departures and the report on enrichment program. Following discussion, the report was approved by signature and there were no minority reports.

Member 10 directed the Committee's attention to the Semi-Annual Inspection Report. The Committee discussed that there were no significant deficiencies and reviewed the plan of action to correct the minor deficiencies including ensuring that hearing protection is readily available when applicable, controlled substance are always securely stored, expired agents are removed promptly, labeling of all containers is appropriate and legible, replacing light diffusers, missing electrical covers, and door labels, removing clutter from fume hood, BSC or procedure rooms, maintaining surgical records and in correct locations, cleaning traps and vents, storing sharps appropriately, removing paper covers for cages, securing all items off floor, assuring that all signage is up to date, clarifying cleaning of behavior equipment, and painting of some rooms and floors. Following discussion, the report was approved by signature and there were no minority reports

b. Review of Guidelines/Policies

The Committee reviewed the following policies and guidelines: ACC updated to for editorial corrections and frequency of retraining, tumor growth and cancer research and updated to clarify the endpoint related to total tumor size, euthanasia of rodents with CO2 and updated to clarify bilateral pneumothorax is required, and definitions guidelines that was updated for references and descriptions. Following discussion, the updates were approved by the Committee by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

c. 19-179 Form H

The Committee reviewed the protocol and discussed that the PI needed to address clarifications listed below. Following discussion, a motion that clarifications are needed to secure approval with designated member review following full committee review for this protocol was passed by the following vote: 7 in favor, 0 opposed, 0 abstentions, and 0 recusals

a. In Form H, item 3, for LCN2 mice, please specifically state which Cre is used and add ERT to the description.
b. In main protocol and Form 4, toe clipping is indicated in main protocol, but is not listed in Form 4. In addition, this procedure is not scientifically justified. PI must work with VA IACUC to reconcile the incongruence between main protocol and Form 4 and if toe clipping will be used justify it. Please contact VA. Once this

issue has been resolved at VA, please submit corrected documents to UIC along with corrected Form H.

d. Modification of Protocol 19-163 (01)

The Committee reviewed the PI's request for 30 athymic nude mice for matrigel assay to investigate the effects of pre-exposing endothelial cells to various levels of LDL on vasculogenesis in an in-vivo model. The Committee discussed that there were no concerns regarding this modification and no clarifications needed. Following discussion, a motion to approve this modification was passed by the following vote: