



Scientific Merit Review

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Qualifications and disclosures



- Animal user within an academic institution
- SHC and NIH grantee; former CIHR grantee
- External reviewer for study sections
- Member of study sections
- ACC member, Chair, University ACC chair
- Ad-hoc member, CCAC assessment committee
- Member of CCAC council (April 2010)

Outline



- Define the issue
- Currently available resources
- Peer-review of grant proposals
- New resources under development:
 - Interpretation bulletin
 - Joint statement
- Key features of the new resources
- Summary/conclusion

Review for animal-based research



- Scientific merit review
vs.
- Review of animal-based methods chosen for the research
 - Same or different?
 - Who is responsible for which?

Currently available resources

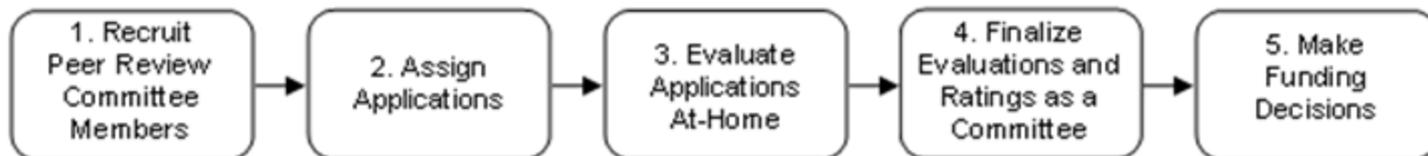


- CCAC policy statement on the importance of independent peer review of the scientific merit of animal-based research projects (2000)
(http://www.ccac.ca/en/CCAC_Programs/Guidelines_Policies/POLICIES/PEER.HTM)
- CCAC policy statement for senior administrators responsible for animal care and use programs (2008)
(http://www.ccac.ca/en/CCAC_Programs/Guidelines_Policies/POLICIES/senior_admin_policy_en.pdf)

Peer-review committees (study sections)



- Reviewers who are experts in the same field (i.e., peers of the applicants)
- Review applications in reference to the evaluation criteria listed in the funding opportunity details
- Provide a numerical rating of the application



Peer-review committees: challenges



- Number of applications to review
- Time constraints for discussion during meeting
- Nature of grant/requested information on grant application form
- Expertise of committee members

Peer-review outcomes



- Written evaluations that include:
 - A brief synopsis of the proposal
 - An assessment of the proposal (strengths and weaknesses)
 - Comments on issues that should be flagged
 - Comments on the budget requested
- Numerical rating of the application between 0.0 and 4.9
- > 3.5 (!) considered for funding.

Peer-review outcomes



- review, by independent, expert peers, of the general research project or program to determine whether the overall proposal has scientific value within its field
- with or without details on animal-based experiments

Peer-reviewed grant applications



- Variable format
 - Number of pages, font size, figures, etc.
- Variable requirements
- Support requested for >1 year:
 - Predict expected results
 - Predict need for animal-based research

CCAC interpretation bulletin



- Explicitly recognizes the need for two necessary levels of review for animal-based research:
 - Scientific value (provided by funding agencies)
 - Review of the animal-based methods chosen for the research (responsibility of the animal care committee within the context of ethical review)

Responsibilities of the institution



- To have in place a mechanism to ensure that a proposed animal use for research is independently peer-reviewed for its scientific merit before it is given final approval by the ACC

Mechanisms for determining scientific merit



- Competitive peer review from funding agencies
 - Funded projects
 - Above-average ratings ('fundable but not funded')
 - Written documentation of internal peer review
- Obtain at least 2 external written reviews
 - Comments addressing:
 - Objectives and contribution to scientific knowledge
 - Appropriateness of experimental design involving animals and animal-based methods

Mechanisms for determining scientific merit



- Corporate scientific advisory board
(external experts bound by confidentiality agreements)

Responsibilities of the researcher



- Choosing the most appropriate methods for their work
- Detailing all animal-based methods in writing to the ACC (animal use protocol form)
- Sharing all relevant information with the ACC (especially if independent, expert peer review has focused on animal-based methods)
- Answer questions from the ACC on any aspect of animal-based work, including:
 - why animals cannot be replaced, if this is the case;
 - why a specific animal model and proposed numbers of animals have been chosen;
 - what refinements to animal use are proposed and what further ones could be considered;
 - what can be learnt from previous, similar work.

Peer-reviewed grant applications

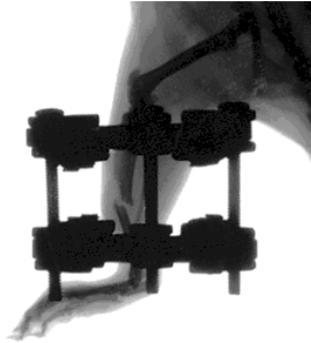


Figure 8: Immobilized fracture based on the distraction osteogenesis mouse model. Osteotomy is performed after the installation of the custom-designed circular external fixators.



Figure 9: Radiograph of fractured femur. The knee joint was flexed and incisions were performed at the level of the patellar ligament. The ligament was dislocated laterally to expose the femoral condyles. A 26G needle was used to make a hole at the head of the femur through which a 25G spinal needle was inserted. The needle was cut and the rodded femur was then fractured with a blunt guillotine. After the wounds were closed, a radiograph was taken to confirm the pin placement and the fracture.

Adult, same gender mice of 4-5 months of age will be used with 6 animals per group. Cohorts will be assigned to collect samples for histology/histomorphometry, while others will be assigned to mRNA isolation for RT-qPCR. A final cohort will be assigned for biomechanical testing at 32 days post-osteotomy. Blood will be collected from all animals at sacrifice to measure calcemia, phosphatemia, and vitamin D metabolite levels. The fractured legs will be dissected at intervals following surgery (14, 21, and 32 days) and fixed overnight in 4% paraformaldehyde. The bones from the day 14, and 21 cohorts will first be analyzed by micro-CT to evaluate bone formation. Then, the fixed long bones will be embedded in methylmethacrylate. Sections of 5 μ m thickness will be deplastified and stained by the Goldner method⁴³ for comparative histology. Quantitative histomorphometry will be performed as described previously^{52, 75, 76} using the BioQuant Osteo histomorphometry system.

Peer-reviewed grant applications



5.5.10 Vertebrate Animals

If vertebrate animals are involved in the project, address each of the five points below.

If all or part of the proposed research involving vertebrate animals will take place at alternate sites (such as project/performance or collaborating site(s)), identify those sites and describe the activities at those locations.

Although no specific page limitation applies to this section of the application, be succinct. Failure to address the following five points will result in the application being designated as incomplete and will be grounds for the PHS to defer the application from the peer review round. Alternatively, the application's impact/priority score may be negatively affected.

The five points are as follows:

1. Provide a detailed description of the proposed use of the animals for the work outlined in the Research Strategy section. Identify the species, strains, ages, sex, and numbers of animals to be used in the proposed work.
2. Justify the use of animals, the choice of species, and the numbers to be used. If animals are in short supply, costly, or to be used in large numbers, provide an additional rationale for their selection and numbers.
3. Provide information on the veterinary care of the animals involved.
4. Describe the procedures for ensuring that discomfort, distress, pain, and injury will be limited to that which is unavoidable in the conduct of scientifically sound research. Describe the use of analgesic, anesthetic, and tranquilizing drugs and/or comfortable restraining devices, where appropriate, to minimize discomfort, distress, pain, and injury.

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5. Describe any method of euthanasia to be used and the reason(s) for its selection. State whether this method is consistent with the recommendations of the American Veterinary Medical Association (AVMA) Guidelines on Euthanasia. If not, include a scientific justification for not following the recommendations.

Responsibilities of the ACC



- As defined by CCAC policy statement on terms of reference for animal care committees
- checking with the research administration to ensure that the corresponding research project/program has received positive peer review
- examining and using any available comments on animal-based methods provided through peer review

Responsibilities of the ACC



- Understanding the methods and make informed choices
 - Experience and expertise of ACC members (scientists and veterinarians) who are familiar with the field in question
- If serious questions remain:
 - consultations with independent experts to gain a better understanding of the methods
 - work with the researcher to arrive at the best possible methods for both ethical and scientific reasons

Summary / conclusions



- The *CCAC interpretation bulletin on: review of scientific merit and animal-based research methods* has been produced by the CCAC Assessment Committee to provide information and assistance to CCAC constituents in addressing the review of scientific merit and of animal-based research methods
- Recognizes two necessary levels of review for animal-based research:
 - **scientific merit review**
 - **review of the animal-based methods chosen for the research**
- research administrations must ensure that research projects have been found to have scientific merit (provide this information to ACC)
- researchers and ACCs are jointly responsible, within the context of the ethical review of animal-based research projects, for ensuring that appropriate methods will be used