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Replacement ♦ Reduction ♦ Refinement

Good Animal Practice in Science



Discussion Paper: Opportunities and Obstacles to Animal Resource Sharing in Canada

Background

Introduction

Animal resource sharing occurs when animal use protocols use: surplus live animals; surplus tissue from animals that have been humanely killed; or animal tissues that are byproducts from an approved protocol and would otherwise go unused.

There are several benefits from animal resource sharing. First, sharing animals and animal tissue contributes to the reduction of the total numbers of animals used in Canadian science. Reduction is part of the Three Rs tenet (along with replacement and refinement) (CCAC, 2012) and is the basis for the [CCAC policy statement on: ethics of animal investigation](#) (1989). Second, animal resource sharing programs can result in more efficient use of animals that are otherwise produced solely to maintain breeding colonies. Third, sharing animal resources can support research innovation by providing quicker and more cost effective access to animal tissue for investigators who wish to carry out preliminary/exploratory investigations prior to applying for a grant.

Method

As part of ongoing efforts to support Three Rs' implementation in Canadian science, the CCAC initiated a project to examine how the sharing of animal resources is carried out in Canadian institutions. To date, there is little published guidance on how to manage animal resource sharing. Therefore, a working group¹ facilitated by the CCAC was established to examine the obstacles and opportunities for sharing animal resources and generate best practice recommendations. Individuals involved in existing animal and tissue sharing programs were consulted about how programs are managed (descriptions of three programs are included in Appendix 2). The resulting best practice recommendations will be published on the CCAC Three Rs Microsite as an information resource for individuals intending to establish an animal resources sharing program at their institution.

¹ Members of the working group included: Jane Alcorn, University Veterinarian and Associate Professor of Pharmacy, University of Saskatchewan; Terry Germscheid, CACS GEMM Coordinator, University of Manitoba; and Robert Madziak, Director CACS (Central Animal Care Services), University of Manitoba.

Opportunities for Animal Resource Sharing

The following opportunities were identified by the working group:

Animals and tissues can often be sourced from existing institutional resources such as breeding colonies or animals “on protocol” for another scientific use. For example when breeding colonies of animals are produced for scientific use, even with careful management, a surplus of animals may be created. Typically the surplus animals are culled and disposed of without being used for any further scientific purposes. These animals are potentially a source of tissue for other scientific protocols. In institutions with a small number of animal colonies to manage, or where there are unusual species, the culled tissue may be frozen for future use. In institutions with a large number of breeding colonies, there is typically an ongoing supply of culled animal tissue and none is ever required to be frozen. Using cull surplus animal tissue does not create an additional ethical “cost” to animals because there is no prior manipulation before death (a death that would occur regardless of whether the tissue is used for scientific purposes). However, if the harvesting of tissues will require modification to the original killing method, then additional animal care committee (ACC) approval may be required.

Additional opportunities for sharing resources can occur when animals that are part of a scientific protocol are humanely killed. This can present an opportunity for the collection of tissues that are not being used by the main study (for example, organ or blood collection). However, if the harvesting of additional tissues will require modification to the original protocol then additional ACC approval is required.

Obstacles for Animal Resource Sharing

Ethical and Regulatory Concerns

Institutions that have attempted to implement animal resource sharing programs identified several ethical and regulatory concerns. These concerns are as follows:

- *Low awareness of the availability of culled animals as a source of tissue:* Both the lack of requirements for reporting breeding colony and colony surplus animal numbers to institutional ACCs and a lack of communication to researchers contribute to a low awareness of the availability of culled animal tissues. This was identified as a particular problem at institutions where the supply of culled animals greatly exceeds current demands for tissue.
- *Uncertainty of ACC processes for use of shared tissue:* This was identified as an uncertainty regarding how to assign a category of invasiveness to protocols using tissue from colony cull animals and uncertainty about requirements for ACC approval and/or assessment of scientific merit prior to using culled animal tissues. It was found that when investigators want to share they may be uncertain whether a protocol amendment is required, or a new protocol, or how they can facilitate “last minute” sharing if it requires alterations to previously approved plans for euthanasia. Resolving these uncertainties is further complicated by the need to ensure any ethical processes are as simple as possible in order to facilitate and encourage sharing.
- *The level of ethical review and approval required for use of banked tissue:* The acceptability of an investigator to run an entire study using only banked tissue or tissue obtained from cull animals, without ever having to file a protocol application may be of concern.

- *A perceived loophole when ACC approval to use culled surplus tissue is not required and investigators hold influence over production of in-house breeding colonies:* Decisions to produce over-produce or delay the termination of a colony could be made by the user simply to offer a potential tissue source from surplus or culled animals. In theory, this tissue could be accessed after the cull without obtaining approval, although approval would be required if the tissue was harvested from animals killed for the specific scientific purpose. This loophole is widened further by the absence of a formal requirement for reporting numbers of breeding colony animals.
- *Lack of widely accepted criteria for: i) breeding colony management best practices, in particular to ensure production is coordinated with animals use; and ii) who should be responsible for making decisions about whether to breed more animals:* Although current CCAC guidelines require that no animal be held except for an approved protocol, there are no criteria regarding what is or is not acceptable for the maintenance of breeding colonies. Where in-house colonies exist, the responsibility and accountability for: the use of best breeding practices; production management (i.e., numbers produced); and assignment and disposition of every colony animal must be clear and subject to the same degree of oversight and scrutiny as any other scientific animal use, through a breeding colony protocol.

Practical Concerns about Implementing an Animal Resource Sharing program

The Three Rs working group identified that the simplest way in which animal resource sharing can occur is when a group of investigators work together and coordinate among themselves. However, for this to happen the investigators must be in close communication and located in physical proximity. Coordination of institution-wide and inter-institutional tissue sharing is recognized to be much more difficult.

For institutions wanting to implement animal resource sharing, the following logistical challenges would need to be resolved to facilitate the process:

- Identification of an individual to coordinate the program.
- Access to an online inventory system that is easy to update.
- Procedures and equipment in place for processing and storing frozen tissue (tissue needs to be categorized, collected and flash frozen at time of collection and stored in a calibrated -80°C freezer with a back-up freezer).
- Ready accessibility for investigators.
- Coordination of supply and demand to ensure surplus animals and/or tissues are available when needed by investigators.
- For genetically-engineered animals (GEA) or GEA tissues, investigators need to consider how the genetic manipulation impacts their use of the animal/tissue and determine whether it is suitable to use it. ACCs may want them to specifically address this point and justify whether it is appropriate. (GEA colonies present a special case because, due to the specificity of the genetic alterations, tissue from these sources may not be suitable for all scientific uses).

- A way to facilitate “last minute” sharing that does not affect, or minimally affects, previously approved plans for euthanasia.
- Methods for documenting the use of cull animal tissues/tissue sharing so the impact of reduction can be measured.

References

Canadian Council on Animal Care (CCAC) (1989) *CCAC policy statement on: ethics of animal investigation*. Available at http://www.ccac.ca/en_/standards/policies/policy-ethics_animal_investigation

Canadian Council on Animal Care (CCAC) (2009) CCAC 5-Year Strategic Plan 2009-2014. Available at http://www.ccac.ca/en_/about/strategic

CCAC (2012) Three Rs Microsite. Available at <http://3rs.ccac.ca/>

Appendix 1

Best Practice Recommendations: Facilitating Sharing of Animals and Animal Tissues

Background

Best practices are shared on the Three Rs Microsite as information that may assist institutions who are looking for ways to further implement the Three Rs in their animal care and use programs. They are not CCAC guidelines documents or policy statements, and will not be used by CCAC assessment panels as a basis for recommendations in assessment reports, (although assessment panels may share the information with institutions as a way to encourage implementation of the Three Rs).

These best practices are for institutions who would like to facilitate the sharing of animals and animal tissue as a means of reducing the numbers of animals used and improving the efficiency of animal use. They were developed by a working group of the CCAC Three Rs Committee and are based on analysis of examples of successful animal and tissue sharing programs (*Discussion Paper: Opportunities and Obstacles to Animal Resources Sharing in Canada*). The aim is to reduce the numbers of animals used, without increasing harms experienced by other animals.

Recommendations

Facilitating Sharing of Animals and Animal Tissue

1. Collect and monitor the number of animals used for breeding and colony maintenance at the institution.
2. Transition to centralization of colony management responsibilities to animal care facilities so as to: enable precise tracking of animals and tissue for sharing; maximize opportunities for use of surplus animals; and minimize over-production.
3. Delegate responsibility and decision-making for colony management to centralized animal care facilities, except in situations where breeding and reproduction is an integral part of the experimental design.
4. Develop criteria on how to identify colonies that no longer need to be maintained.
5. Prepare an institution-wide animal use protocol to cover use of surplus animal tissues.
6. Permit a type of protocol where a principal investigator can wait for a cull animal (surplus animal already destined to be killed) to become available.
7. Provide scientific justification on animal use protocol applications for why surplus tissues or animals cannot be used.
8. Provide dedicated funding to cover costs of coordinating an animal resource sharing program.
9. Provide access to the surplus resources at no or low cost to investigators.
10. Create a plan to advertise and raise awareness of this source of animal tissue and encourage investigators to use surplus tissue first and to donate resources (i.e., generating a demand for the tissue).

Appendix 2

Examples of Animal Resource Sharing Programs

Example 1: University of Manitoba

The University of Manitoba animal facilities actively attempts to provide investigators with tissues from surplus, culled animals. Investigators are asked on animal care protocols about whether they would use or donate cull tissues. Although many investigators indicate ‘yes’, this is logistically difficult to coordinate. At present the surplus tissue is not frozen as the supply of fresh tissue greatly exceeds the current demand.

The University of Manitoba has several policies that help to facilitate tissue sharing. It collects data on the number of animals produced in its breeding colonies and reports the numbers produced, used and culled to its animal care committee (ACC). It requires that new genetically-engineered animal colonies be centrally managed unless there is a scientific reason for a principal investigator to manage them separately. The ACC has also developed an internal guideline on colony management issues that are not covered by CCAC, including guidance on setting production levels and how long to maintain a line of animals.

Example 2: SEARS and STORE Programs at UCLA

Four years ago, the University of California Los Angeles (UCLA) began the Surplus Experimental Animal Resource Sharing (SEARS) Program and the Sharing Tissues and Organs for Research Excellence (STORE) Program. When these first started, they were funded by the UCLA medical school and the Division of Laboratory Animal Medicine. First, the animal care facility wrote a “holding protocol” to allow investigators to retain their surplus animals. The per diem cost of keeping the animals was paid by the SEARS program; approximately 50 or 60 cages of animals were held in surplus per month. The STORE program coordinated the sharing of tissues from freshly killed animals. The tissues were never frozen.

Animal availability was initially communicated to UCLA investigators in a monthly emailed newsletter. Investigators also began emailing the facility veterinarian with requests. There was a high level of interest and participation in the program, and managing the communications took up too much of the facility veterinarian’s time. The work of coordinating donations and requests for animals was then delegated to student volunteers.

Next, an online software platform to manage both programs was developed by adding on to the existing online Institutional Animal Care and Use Committee (IACUC) system, using the same security features. Individuals with passwords can access the surplus animal listings and post ads for available surplus animals, along with expiration dates. Investigators can also prospectively posted the dates that they will be sacrificing animals and what tissues will be available for others. Investigators may directly contact one another; however, they are also required to complete a tissue sharing form to file with the IACUC.

Funding for per diems ran out and now investigators must themselves pay for holding surplus animals. Although the effect of the STORE and SEARS programs is not formally monitored, the facility veterinarian estimates that in the beginning (when per diems were funded) annual animal orders declined (estimate reductions of 1000 rats/year, 1000 mice/year, 6 pigs/year). With no funding, participation in SEARS and STORE has declined (possibly by 50%).

Surplus Experimental Animal Resource Sharing (SEARS)
<http://vmp.healthsciences.ucla.edu/research/surplus-animals/>

Sharing Tissues and Organs for Research Excellence (STORE)
<http://vmp.healthsciences.ucla.edu/research/store/>

Example 3: Shared Ageing Research Models (ShARM)

Shared Ageing Research Models (ShARM) (<http://www.sharmuk.org/>) is a not-for-profit UK organisation, open to all scientific investigators in the UK and overseas. It was officially launched in July 2012. ShARM has the following services:

- 1.** Biorepository provides acquisition, storage and provision of flash frozen, aged murine tissue
 - Samples from a range of models and ages with an online inventory and young controls available.
 - Housed in dedicated space of a large scale biorepository with 4 cryogenic tanks and 43 -80°C freezers with a total capacity of more than 1.5 million samples.
 - Liquid Nitrogen supply is automated and the whole facility is secured and monitored 24/7 by an outside control room and the person responsible is immediately notified if a problem is detected.
 - Storage is controlled by a highly secure database with standards compliant for the Human Tissue Authority (HTA) regulations for biobanking.
 - Database recognises each individual tissue with a barcode.
- 2.** Live Ageing Colony database
 - Provides online, searchable database of current, live ageing colonies.
 - Colony owners are invited to register their colony for addition to the database and are introduced to investigators able to use surplus tissue.
- 3.** MiCESPACE online forum
 - Promotes the networking of researchers and dissemination of knowledge through online, collaborative environment (not yet launched).

ShARM was established in collaboration by MRC Harwell (UK Medical Research Council mouse genetics research centre) and the Centre for Integrated Research into Musculoskeletal Ageing (CIMA) (collaboration between Universities of Sheffield, Newcastle and Liverpool) following an application for funding from UK's Wellcome Trust. It is overseen by a board of managers that consist of 5 permanent members (grant applicants) and 4 investigators from the research community who are elected and serve for 2 years. It employs 2 members of staff (a facility coordinator and IT manager).