Module 01 - Guidelines, Legislation, and Regulations Regarding the Use of Vertebrate Animals in Teaching and Research

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The first written standards for the care and use of experimental animals in Canada were developed in1961 by a committee of the Canadian Federation of Biological Societies - *Guiding Principles on the Care of Experimental Animals*. A few years later the Medical Research Council and the National Research Council undertook a study to look at the question of how national standards for experimental animal care and use should be implemented. The report came back recommending that the Canadian Council on Animal Care (CCAC) be established, to provide guidance for all aspects of the care and use of experimental animals. The Canadian Council on Animal Care (CCAC) was founded in 1968 as a standing committee of the Association of Universities and Colleges of Canada. Following the recommendations in the report, Canada opted for a peer review system based on guidelines. The system was selected to draw on the strengths of many organizations to reach its goals. The Canadian Federation of Humane Societies was included from the outset as a representative of the animal welfare movement in Canada. In this system, the CCAC pioneered the establishment of local animal care committees responsible for the ethical use of animals at their institutions. There are now more than 220 Animal Care Committees (ACCs) across Canada. Since 1968, the CCAC program has brought about high standards for experimental animal care and use through education, voluntary compliance and a code of ethics. General and specific guidelines have been written, revised and expanded in response to changes in scientific and ethical attitudes to the use of animals in research, teaching and testing. Such "living" documents as the standards for the CCAC program have been a model for exemplary animal care and use throughout the world, and have been emulated in several countries.

What is the Canadian Council on Animal Care?

The purpose of the Canadian Council on Animal Care is to act in the interests of the people of Canada to ensure through programs of education, assessment and guidelines development that use of animals, where necessary, for research, teaching and testing employs optimal physical and psychological care according to acceptable scientific standards, and to promote an increased level of knowledge, awareness and sensitivity to relevant ethical principles. The

"council" is the governing body of the CCAC. It consists of representatives of a wide range of national organizations with an interest in the care and use of animals in research, teaching and testing.

Supporting the work of the Council are five standing committees, with additional experts that serve on specific committees (e.g., *ad hoc* subcommittees are established when new guidelines are being developed or old ones revised). The Council is supported by a secretariat (an office staff) in Ottawa, which coordinates the many aspects of the national program of standards for the care and use of experimental animals. At the inaugural meeting on January 30, 1968, the CCAC adopted the following statement of objective: "to develop guiding principles for the care of experimental animals in Canada, and to work for their effective application". These guiding principles contain the fundamental requirements for humane and ethical use of animals in research, teaching and testing in Canada.

To carry out its mandate, the CCAC adopted a decentralised model in which responsibility for all matters relating to the care and welfare of experimental animals resides within the institution - through the animal care committee. The CCAC provides the national standards through the various guidelines and through its Assessment Program, evaluates the work of the animal care committees and monitors compliance with the national standards. It is essential that the institution be committed to the CCAC standards for physical infrastructure, animal care and protocol review. These aspects of the CCAC program are discussed in more detail in following sections.

Guidelines of the CCAC

Since the first *Guide to the Care and Use of Experimental Animals* was published in 1968, the guidelines of the CCAC have steadily evolved in response to new information or requirements that address new research or ethical needs. The most recent general guidelines document is the *Guide to the Care and Use of Experimental Animals* Volume 1, 2nd Edition, 1993. This volume along with the currently approved CCAC guidelines is available on the CCAC website (**www.ccac.ca**). It became clear during the 1990s that there was a need for more specific guidelines in certain areas, and so the CCAC embarked on a program to publish individual guidelines on selected topics. The development of these specific guidelines involves the establishment of small *ad hoc* subcommittees to draft the guideline document. Once a draft is

ready, there is widespread consultation throughout Canada to achieve a consensus on the information in the guideline. For example, new guidelines are posted on the CCAC website in draft form to allow people to comment on them. Thus, as many people as possible are encouraged to participate in the development of guidelines.

The Institutional Animal Care Committee

The Animal Care Committee (ACC) in each institution has a number of responsibilities relating to the care and use of animals in research, testing and teaching. These responsibilities are detailed in the CCAC publication entitled *Terms of Reference for Animal Care Committees.* The following is an overview of the major responsibilities of an Animal Care Committee.

Review and approval of all proposals to use animals:

The ACC must ensure that every proposal to use animals for teaching, testing or research has been reviewed both for scientific merit, and for compliance with accepted ethical standards (see Module 02). Each protocol must be the subject of an annual review, and any amendments reviewed and approved.

Authority:

As defined in the CCAC Terms of Reference for Animal Care Committees, the ACC has the authority to halt any study that deviates from the approved protocol or where the animals are found to be suffering excessive pain or distress that cannot be relieved. In the latter case, an animal may be euthanized if the pain or distress cannot be relieved in any other way. Usually the veterinary staff is given this authority on behalf of the ACC.

Ensuring standards for animal facilities and care:

The ACC must ensure that facility standards and the care of the animals are in accordance with the CCAC Guidelines, and that a qualified person has been clearly designated to be responsible for the day-to-day facility management and animal care.

Prevention and relief of pain and distress, and ensuring adequate veterinary care:

The ACC must ensure that adequate veterinary care is provided, and that appropriate procedures are in place to ensure that unnecessary pain and suffering do not occur.

Ensuring the training and skills of all persons working with animals used in science:

The ACC must implement a program to ensure that all persons working with animals receive practical skills training, in accordance with the CCAC guidelines.

Membership of the ACC:

To ensure that the well-being of the animals is fully considered, the ACC needs to have a membership with a broad representation of interests and expertise. This broad representation is reflected in the membership requirements found in the CCAC Terms of Reference for Animal Care Committees. A properly constituted ACC must have:

- Scientists and /or teachers experienced in animal care and use
- Veterinarian(s) experienced in animal care and use
- An institutional member whose normal activities do not involve animals
- At least one person representing community interests and concerns who does not have any links with the institution or with animal use for research, teaching or testing.
- Technical staff involved in animal care and use
- Student representation in academic institutions
- Animal facility managers

The number of people from each category will depend on the size of the institution and its animal use program. The ACC must have active support from the administration of the institution, including adequate office and secretarial support to fulfill all its responsibilities both to the institution and to the CCAC. Documenting all ACC actions and activities is very important. The ACC is required to maintain certain documentation regarding the animal care and use at the institution, and must provide the CCAC with annual reports of animal use, and other specific information prior to a full CCAC assessment.

Protocol Review

The review of proposed animal use before it begins is one of the fundamental pillars of the CCAC program and it is the most important responsibility of the ACC. The CCAC has a number of documents and guidelines that assist the ACC in fulfilling this important responsibility before a request to use animals in research, teaching or testing can be approved, the protocol reviewers should be able to satisfactorily answer a series of questions such as:

- **Do you understand why the study should be done?** The scientist proposing the animal use should have explained, in language easily understood by every one of the reviewers, including the non-scientific members, the potential benefits, for people or animals, arising from the study.
- **Are you convinced that animals must be used?** The scientist proposing the animal use should have convincing arguments that there is no other way to obtain the information being sought in the study.
- **Has the proposal been independently reviewed for scientific merit?** If this has not been done, the ACC will take steps to ensure that a peer review for scientific merit is undertaken. Approval to use animals requires that the use is ethically acceptable and scientifically meritorious.
- **Has the concept of the Three-Rs been addressed?** The scientist proposing the study or teaching use of animals must indicate the steps taken to refine procedures and to reduce or replace animals in the study.
- **Has the choice of animal species and model, and the number of animals requested been justified?** Not all species are suitable for all studies. The number of animals requested should fit the proposed experimental design. Are there too many animals or perhaps not enough? (Statistical justification should be provided.)
- **Do you understand exactly what will be done to each animal and in what sequence?** The description of the procedures should be clearly written in understandable language. For example, volumes of injections or samplings, and their frequency should be presented in the written protocol, along with a plan for animal monitoring.
- **Are you comfortable that the expertise of the people carrying out the procedures is optimal?** Will additional training or help be required to carry out the project?

- **Are the facilities for performing the study suitable?** Are the facilities appropriate for housing the species proposed? Will there be environmental enrichment for the animals? Are surgical facilities available? What about suitable anesthetic equipment?
- **Have the signs of pain, stress or distress been described?** Are there measures to relieve these signs, including euthanasia? Humane endpoints should be identified, particularly when it is known that pain and distress are likely to occur, but also when there is the possibility of inadvertent animal injury or pain and/or distress.
- **Will euthanasia be carried out in an appropriate, approved manner?** Do the people involved have the necessary skills to perform euthanasia? The question should provide a sense of the role that members of an ACC have in evaluating the acceptability of a proposal to use animals in research, teaching or testing.

Animal Facility Visits by the ACC

Inspecting all animal facilities at least once each year is an important responsibility of the ACC. These inspections ensure that animal care or facility problems are identified and resolved. The ACC's facility inspection reports are reviewed by the CCAC assessment panels when they visit the institution, and this review allows an assessment panel to target problem areas. This approach enables the CCAC to provide positive feedback and support to an institution while maintaining institutional responsibility for quality control of its animal care and use program.

Developing and Approving Standardized Procedures (SOPs)

Written Standard Operating Procedures (SOPs) are common in many work areas. This is an excellent mechanism for ensuring that work procedures are consistently done regardless of who performs the work. Within animal facilities the implementation of approved SOPs for the care and use of experimental animals and for facility management helps ensure that the treatment of animals in all phases of research, teaching and testing is of a high standard. A major advantage of approved SOPs is that they may be quoted within a protocol submission as an indication to the ACC that the procedures will be carried out in an approved manner. Properly written, approved SOPs provide an easily understood outline of what exactly will be happening to an animal in a research protocol, thereby assisting the ACC in its review of the protocol, and reducing the work required by protocol authors.

The Role of the Principal Investigator in Ensuring Responsible Experimental Animal Care and Use.

Each individual involved in a project using animals is responsible for the well-being of the animals. The principal investigator has the added responsibility of fostering a responsible caring attitude towards the animals in the conduct of the research. This extends to all aspects of the project so that at the end of the day, no animal derived data has to be discarded because of lack of care or foresight. This principle should also govern the actions of all the members of the research team. The principal investigator must ensure that the team is following his/her example.

The CCAC Assessment Program

The CCAC Assessment Program is peer review-based, and depends on the active involvement of scientists on CCAC assessment panels, sharing their expertise and experience with the members of the institution being assessed. Scientists also play a crucial role on the CCAC Assessment Committee, a standing committee that reviews all CCAC assessment reports and institutional implementation reports, and makes final decisions on the CCAC status of each institution in the Program. A key element of the CCAC system is the involvement of the public in all of the CCAC's activities, namely in establishing ethical standards through guidelines development, in ethical decision in-making at the level of each institutional ACC, in providing sound judgment on each CCAC assessment panel, and in providing a public perspective on the CCAC Council. This integrated approach is essential to ensure that an external perspective is actively provided to all discussions and decisions on animal care and use in science, and that those who conduct the experiments are in tune with their obligations to the animals in their care, as well as to the other members of society.

The CCAC assessments serve as the quality assurance program for the institution's Animal Care Committee (ACC) and all aspects of an institution's animal care and use program. It is the primary means whereby the CCAC receives assurance that the national standards - the CCAC guidelines and policies - are being met. Two types of assessment may occur: a formal, announced full assessment of an institution's animal care and use program, and unannounced or other special visits (usually by a CCAC Assessments Director) to deal with specific areas of concern that need to be resolved.

Assessment Frequency

Institutions are formally assessed every three years. Institutions found to be in full Compliance for two successive full assessments may be placed on a five-year cycle by the CCAC Standing Committee on Assessments. Special visits may occur at any time and at any frequency required by the CCAC to ensure that the level of animal care and use meets its standards.

The CCAC Assessment Panel

The members of an assessment panel are selected based on their expertise in animal care and use and in the areas of research and teaching taking place at the institution. An assessment panel is usually composed of a veterinarian, at least one scientist, and a community representative nominated by the Canadian Federation of Humane Societies. These assessment panel members provide their time voluntarily; only their expenses are covered by the CCAC budget.

The CCAC Assessment Process

When a formal assessment is due, the institution is asked to provide each panel member with all the required information about the administrative organization, animal care personnel, veterinary care program, animal care and use practices, and the animal facilities (i.e., a pre-assessment document). This documentation allows the panels to develop a clear idea of the functioning of all aspects of the animal care and use program at the institution and permits more focused probing of areas of concern. Further information can be found at: www.ccac.ca

The Site Visit

When an assessment panel arrives at an institution, there is usually a meeting with the ACC, senior representatives of the administration, animal users and care-givers. During this meeting the panel explores various aspects of the animal care and use program and clarifies any areas of concern identified in the pre-assessment documentation. Broadly, the assessment panel reviews five program areas:

• Functioning of the ACC

• Animal holding facilities
• Animal care and management practice
• Veterinary care program
• Continuing education and training

In any of these five areas, any recurring deficiencies might be symptoms of a problem that needs to be identified and resolved. Following the initial meeting, all locations at the institution where animals are held and used are visited. Usually a senior technician working in the area and one or more of the scientists will accompany the panel. The panel may ask to speak with individual scientists regarding their studies, and must be given access to any protocol or SOP of interest. Once the site visit is completed, the panel meets to formulate the recommendations that will be made to the institution (usually to the senior administrator responsible for the animal care and use program), particularly those of a major or serious nature. At this final meeting, the Chair of the panel will present any recommendations to be made. This is an important meeting in that it should allow the panel to clarify any possible misapprehensions gained through the pre-assessment documentation or during the site visits.

The Assessment Report

The final wording and recommendations contained in the assessment report are prepared at the CCAC secretariat, then sent to the assessment panel and the CCAC Assessment Committee for final review and approval. On its recommendation, the report is sent to the institution. The report is a confidential document to the institution. However the institution may choose to release all or part of it following written notification to the CCAC. The assessment report usually contains recommendations to which the institution must respond within a specified time period. Serious or Major recommendations relate to situations that impose an immediate threat to the well being of the animals, and these problems must be corrected within a short time frame (some may need immediate correction and others within three months of receiving the report). Regular recommendations point to things that may not pose an immediate threat to the animals but need to be corrected in due course and not left to deteriorate (e.g., facility maintenance). A plan for the correction of these problems must be submitted within six months of receiving the Assessment Report

The Follow-Up

When an institution submits its Implementation Report, it is reviewed by this same Assessment Committee and assessment panel. If the report is acceptable, the institution will be assigned a status of "Compliance" or "Conditional Compliance" and given a certificate of Good Animal Practice®. If all or parts of an Implementation report are not accepted, further action is taken.

Compliance and Non-compliance

The CCAC Policy on Compliance and Non-compliance defines four statuses that can be assigned to an institution: Compliance; Conditional Compliance; Probation, and Non-compliance. The most serious situation would occur when an institution is placed in a status of "Non-compliance". If no timely resolution of the situation is found, the CCAC policy states that the granting agencies will be notified, and the granting agencies in turn have agreed to withdraw research funding from the noncompliant institution.

Legislation in Canada Related to Experimental Animals

Federal Legislation and Regulations

A legal opinion commissioned by the CCAC in 1998, Legislative Jurisdiction over Animals Used in Research, Teaching and Testing and an independent study commissioned by Health Canada in 2000, The Protection of Animals Used for the Purpose of Xenotransplantation in Canada, both reach the conclusion that under the Constitution Act 1867, the federal government does not have jurisdiction to legislate with respect to experiments involving animals as this is a provincial jurisdiction. However, the federal government is not totally absent from the field of animal welfare. The three areas in which the federal government has taken action are under the criminal law power, the health power and the spending power.

The Criminal Code of Canada

Section 446 and 447 of the *Criminal Code* protect animals from cruelty, abuse and neglect. This section of the Criminal Code has been under review for several years.

The Health of Animals Act

The Health of Animals Act (1990) and its regulations are aimed primarily at protecting Canadian livestock from a variety of infectious diseases that would threaten both the health of the animals and people, and Canadian trade in livestock with other countries. This act is used both to deal with named disease outbreaks in Canada, and to prevent the entry of unacceptable diseases that do not exist in Canada.

The Spending Power

The other mechanism through which the federal government has lent its support to the humane treatment of animals is not strictly speaking legislative in nature, but in many respects it is one of the most powerful instruments available to the federal government for setting national standards. The federal government's power to provide for grants subject to conditions imposed on the recipients be they provincial governments or individual or corporate recipients may take a variety of different forms. One form is that of the conditional federal grant or contract. This manifestation of the federal power is what currently underpins the imposition of CCAC standards on facilities receiving funding from the Canadian Institutes of Health Research and the Natural Sciences and Engineering Research Council. Where the government itself awards a contract on an academic or non-academic institution, clause A9015C of Public Works Standard Acquisition Clauses and Conditions Manual imposes conditions related to the care and use of experimental animals in public works and government services.

Provincial Legislation and Regulations - Ontario

While all of the provinces have legislated in the area of animal welfare in some form or another, only certain provinces have specifically occupied the field of animals acquired and used for research, teaching and testing purposes. The Ontario legislation, namely the *Animals for Research Act*, is unique in Canada in that it creates a system of control based on the registration of research facilities and the issuance of licences for supply facilities. In Ontario, therefore, all research facilities that use animals in their work must be registered. Among the provisions of the *Animals for Research Act*, one should note the duty to establish an animal care committee, the responsibilities and powers of which are similar to those required under the CCAC system, and

the requirement for any operator of a research facility to submit to the person designated by the Minister of Agriculture, Food and Rural Affairs a report respecting the animals used in the research facility for research. The regulation *Research Facilities and SupplyFacilities*, also provides minimum standards for the housing and care of animals and the regulation *Transportation*, prescribes the conditions for transporting animals used or intended for use by a research facility

Other Interests Affecting Experimental Animal Care and Use

The media have an interest in research in general, and biomedical research in particular. A publication in a journal may stimulate interest from the media and a discussion of animal use in research may ensue. Institutions and investigators should be prepared, through a carefully thought out institutional communications plan, to explain their use of experimental animals, including the procedures and safeguards in place to ensure that the animals were not subjected to any unnecessary pain and/or distress. Maintaining a dialogue with all persons interested in animals is an approach that is fundamental to the CCAC philosophy