

The institutional animal care committee: Keystone of international harmonization

Clément Gauthier

Canadian Council on Animal Care
1510-130 Albert Street, Ottawa, ON, Canada K1P 5G4
cgauthier@ccac.ca

Abstract

The various national systems of oversight for the care and ethical use of animals in science have many fundamental elements in common including: regulations/guidelines/policies, and training requirements for key staff. Authorization of animal use may occur centrally as in the UK, regionally as in several European countries, or locally, through institutional Animal Care Committees (ACCs), as in Canada, US and Australia. Canada is recognized as having pioneered the establishment of ACCs as the keystone of peer-based ethical review processes and local quality control.

The institutional ACC has a central role to play in the international harmonization of standards because: it is representative of the scientific culture and moral values of home countries; it facilitates communications and empowers informed decision-making at the local level; it is already integrated as an accountable keystone of most national oversight and regulatory systems worldwide; and it provides each nation with enhanced ability to influence international harmonization of best practices for animal care and use in science.

Keywords: harmonization, animal care committee, oversight

Introduction

The principles of humane science, encapsulated as the Three Rs (Russell & Burch, 1959), have become enshrined in legislation regulating the use of animals for scientific purposes in several countries. While the various national systems of oversight may appear to be quite diverse in operation, they have many fundamental elements in common, including: regulation, guidelines and policies which impact on the place, the program of work, the personnel involved, and the training requirements for key staff. Responsibility for the authorization to carry out animal-based studies may be invested centrally as in the UK, regionally as in several European countries, or locally, through institutional ACCs, as in Canada, US and Australia (Gauthier & Griffin, 2005).

Since 1968, the CCAC has been the national peer-based organization, involving over 2,000 scientists, veterinarians, animal care staff, students and representatives from the public and animal welfare movement, with the responsibility for establishing and maintaining standards (its guidelines and policies) for the care and use of animals in science. CCAC also bears the responsibility to ensure that its guidelines are harmonised with those of the international community.

Gauthier & Griffin (2004) have pointed to the need for international harmonization of standards

as a priority because of: broad implications for international scientific collaborations; global acceptance of research data; and international trade. As opposed to international standardization, the international harmonization of guidelines implies an approach based on common shared knowledge, and that is respectful of cultural and other international differences; this must be recognized in considering adoption of guidelines from other jurisdictions.

Canada is recognized (Orlans, 1989) as having pioneered the establishment of ACCs as the keystone of its ethical review and oversight system for the use of animals in science. In Canada, there are over 220 ACCs, each structured as a microcosm of society, including local community representatives, veterinarians, scientists, animal care staff and students. They are established under the *CCAC policy statement on: terms of reference for animal care committees* (CCAC, 2006a) to ensure local quality control, with the CCAC at the national level providing quality assurance of institutional animal care and use programs. Whether they are called institutional animal care and use committees (IACUCs), ACCs or Ethical Review Processes, ACCs are now an essential part of oversight systems worldwide, irrespective of the voluntary or legislated frameworks in place in different jurisdictions.

International harmonization

Endpoints: An example of international harmonization post factum

Categories of Invasiveness (CI) describing the potential level of pain and distress that could be experienced by animals involved in experimental procedures, were developed by the CCAC in 1988, and revised in 1991 (CCAC, 1991). In 1996, the CCAC began to report numbers of animals used according to five purposes of animal use. In 1997, it was found that 29% of animals used in Canada for research, teaching and testing experienced moderate to severe pain and/or distress, CI D and E on the CCAC five point scale. It is for these types of studies that the *CCAC guidelines on: choosing and appropriate endpoint in experiments using animals for research, teaching and testing* (CCAC, 1998) were developed. The guidelines provide a specific definition of an endpoint and give specific guidance establishing earlier endpoints, recognizing the following areas where earlier endpoints are desirable:

- Monoclonal antibody production
- Cancer research
- Acute toxicity testing in mammals
- Acute toxicity testing in fish
- Chronic toxicity studies
- Aging
- Pain research
- Infectious disease studies, vaccine trials, etc

The purpose of the guidelines was (i) to provide guidance for selecting an endpoint that reduces the potential for animal pain and/or distress, whilst still satisfying the experimental design requirements for objective evaluation, and (ii) to assist institutional ACC members and investigators in fulfilling their ethical responsibilities in minimizing animal pain and/or distress. Key provisions of the guidelines include: recommended procedures for selecting an appropriate endpoint; using preliminary or pilot studies to determine the appropriate endpoint; determining the required frequency of animal observations; defining responsibility for animal observations; and training of personnel in clinical animal observations.

At the national level, the implementation of these guidelines elicited the validation of non-lethal endpoints for five biologicals by Health Canada (Calver et al, 1999), and resulted in a 50% decrease in the numbers of animals reported to be used under Category of Invasiveness E. Most importantly, as evidenced at the time of CCAC assessment visits of institutional animal care and use programs, the implementation of the guidelines has increased the attention paid by animal users to animal well-being and has fostered a team approach involving scientists, veterinarians, animal care technicians and ACC members.

At the international level, the *CCAC guidelines on:*

choosing and appropriate endpoint in experiments using animals for research, teaching and testing (1998) were recognized as effective refinement tool with the *OECD Draft Guidance Document on the Recognition, Assessment and Use of Clinical Signs in Humane Endpoints for Experimental Animals Used in Safety Evaluation* (Organisation for Economic Cooperation and Development, 1999), at the 1999 Third World Congress on Alternatives and Use of Animals in Life Sciences (Griffin and Koeter, 2000).

The *CCAC guidelines on: choosing an appropriate endpoint in experiments using animals for research, teaching and testing* (1998) emerged as a flexible basis for harmonization worldwide at the June 2001 International Symposium on Regulatory testing and Animal Welfare organized by the CCAC in collaboration with the International Council for Laboratory Animal Sciences (ICLAS). This symposium was a premiere in sharing best practices on endpoints at an international level in relation to invasive protocols. It attracted 160 scientists, regulators and animal welfare representatives from 22 countries and resulted in published proceedings in the *ILAR Journal* including specific recommendations on the implementation of current best scientific practices relating to endpoints as well as requirements for future progress (Combes et al, 2002). The first ICLAS international meeting for the harmonization of guidelines held in Nantes, France in 2004 resulted in the recognition of the CCAC and OECD documents on endpoints as international reference documents, and in the publication of ten general principles for the establishment of humane endpoints based on these two documents (Demers et al, 2006).

Euthanasia: Harmonization through adoption of internationally recognized documents

As opposed to international standardization, the international harmonization of guidelines implies an approach based on common shared knowledge, and that is respectful of cultural and other international differences; this must be recognized in considering adoption of guidelines from other jurisdictions.

The harmonization of guidelines on euthanasia was the second issue addressed by the ICLAS Working Group on Harmonization of Guidelines resulting in the publication of ten general principles for euthanasia (Demers et al, 2006) on the basis of two international reference documents, namely the *Report of the American Veterinary Medical Association (AVMA) Panel on Euthanasia* (2000) and the *European Commission recommendations for euthanasia of experimental animals* (1996/1997). The CCAC developed its adopted guidelines on euthanasia using the following process which is suggested as a general approach to adopt and modify guidelines from other jurisdictions to fulfill national needs and support

international harmonization.

- Guiding principles developed by an ICLAS Working Party.
- Evaluation of existing guidelines by a national subcommittee for consideration for adoption and identification of gaps. As opposed to standardization, harmonization requires careful consideration of national regulations and culture.
- Development of an upfront statement and the necessary justification to facilitate the implementation of the adopted guidelines by local, institutional ACCs.

The ACC: Keystone of international harmonization

While an effective harmonization platform, such as the ICLAS, is a key structural element of the harmonization process at the international level, the keystone of the whole enterprise remains the local, institutional ACC. International harmonization of standards is needed, not international standardization. In that process, the institutional ACC has a central role to play because:

- It is representative of the scientific culture and moral values of home countries;
- it facilitates communications and empowers informed decision-making at the local level;
- it is already integrated as an accountable keystone of most national oversight and regulatory systems worldwide; and
- it provides each nation with enhanced ability to influence international harmonization of best practices for animal care and use in science.

1. Reflecting national culture and values through community representation on ACCs

Mautner (1996) defines ethics as the predominant community spirit. It is in this vein that ACCs are able to move beyond the continuing polarized debate on the use of animals in science, to a more enlightened public engagement in concrete, informed ethical decision-making on specific protocols. The *CCAC-CFHS Manual for Community Representatives* (2006b) is a comprehensive document detailing the characteristics, selection, term, roles and responsibilities of community representatives on ACCs. A summary is provided below.

Characteristics, selection and term

Community representatives come from all walks of life; they can, for example, be members of a humane society, retirees, lawyers, homemakers, business people, teachers, ethicists, or members of the clergy. Community representatives can have any background as long as they do not use animals for

scientific purposes, they are not affiliated in any way with the institution that they will be working with, and they do not have any conflict of interest that would compromise their role. Their most important qualifications are to be actively interested in the care and use of animals, to be willing and able to work constructively with the members of animal care and use programs to address ethical dilemmas posed by science, and to be ready to undertake a certain amount of work and learning, depending on the size and complexity of the institution that they will be working with. Community representatives are selected either by the members of institutional ACCs, or by the institution itself in collaboration with the ACC. Like other ACC members, they are appointed for terms of no less than two years and no more than four years, renewable only up to a maximum of eight consecutive years of service.

Role and responsibilities

The role of community representative on an ACC requires a considerable time commitment and is usually non-remunerative. A new community representative must invest time to learn about the ACC's functions by reviewing: the Terms of Reference of the ACC; minutes of the past year's meetings; and institutional policies and procedures relating to the animal care and use program. The community representative must also become knowledgeable about: the mandate of the institution and its organization; the type of research, teaching or testing carried out at the institution; and CCAC policies and guidelines.

On an ongoing basis, the responsibilities of the community representative include: reviewing all animal use protocols and other ACC documents; being present at ACC meetings and other activities; participating actively in the protocol review process; touring the animal facility at least once a year; participating in the development and review of institutional animal care and use policies and procedures; and being present for CCAC assessment visits.

2. Facilitating communications and empowering informed decision-making

As per the *CCAC policy statement on: terms of reference for animal care committees* (CCAC, 2006a), the primary role of a community representative on an ACC is "to participate actively in decision-making on the care and use of animals, through working with the members of an institution and its ACC to ensure good animal care and use at the institutional level".

The functioning of the ACC is the first element evaluated by the CCAC assessment panel during an assessment visit. A key criterion is the level and depth of exchanges between community representatives and

the other members of the committee reported in the minutes of their deliberations, and their impact on the decision made on specific protocols.

3. Integrated to most national oversight and regulatory systems

The various national systems of oversight for the care ethical use of animals in science have many fundamental elements in common including: regulations/guidelines/policies, and training requirements for key staff. Authorization of animal use may occur centrally as in the UK, regionally as in several European countries, or locally, through institutional ACCs, as in Canada, US and Australia. Nonetheless, all the above countries have incorporated the concept of the ACC to their structure (Gauthier and Griffin, 2005).

For example, the US *Animal Welfare Act* 1966 enforced by the US Department of Agriculture was amended in 1985 to establish the institutional Animal Care and Use Committees (IACUCs). In the same vein, the UK *Cruelty to Animals Act* 1876 was repealed by the *Animal (Scientific Procedures) Act* 1986 which is enforced by the Home Office (HO) inspectors. Since 1999, each establishment is required to have in place an Ethical Review Process (ERP) as a condition on all certificates of designation issued by the HO. Canada pioneered ACCs as the keystone of its decentralized oversight system in 1968. Participation in the CCAC programs is mandated through federal spending power for academic institutions and voluntary for government and industry; however, CCAC standards are referenced in regulations to provincial laws and relevant federal departments' policies and regulations, making it a quasi-regulatory body.

A statistical trend analysis study (Gauthier, 2004) using original data on animal use published between 1980 and 1999 by the UK Home Office, the US Department of Agriculture and the CCAC showed that a sustained downward trend of similar magnitude occurred in the UK, US and Canada throughout the 1990s, demonstrating their equivalent effectiveness in implementing Reduction measures. This is an interesting observation, in view of the fact that while the UK system of oversight is legislated, Canada has evolved a non-legislated system due to the fact that animal welfare is not a federal but a provincial jurisdiction. The US have evolved a hybrid system involving both legislations and voluntary compliance, an approach also adopted by several European and Asian countries.

4. Providing each nation with enhanced ability to influence international harmonization

As demonstrated above, the *CCAC guidelines on: choosing an appropriate endpoint in experiments*

using animals for research, teaching and testing (1998) emerged as a flexible basis for harmonization worldwide, as a result of sharing best practices developed by ACCs in implementing these guidelines. After having thoroughly reviewed the best scientific practices for animal care committees and animal use oversight, participants in the ICLAS-CCAC International Symposium on Regulatory Testing and Animal Welfare (Richmond et al, 2001) concluded:

"Experience has shown that different frameworks [voluntary or legislated] provide effective oversight in different jurisdictions and within organizations with different cultures. Indeed, providing the process works in practice, diversity, which can of itself promote continuous improvement, should not be discouraged."

"Future progress requires the following: encouraging diversity; networking ACCs to identify, encourage and share best practices."

Conclusion

Animal care committees, including membership from investigators, veterinarians, animal care technicians, community representatives, and animal welfare representatives can bring a broad spectrum of community views about the use of animals to bear on a practical case-by-case use of animals. However, there must also be some form of national oversight mechanism in place to provide quality assurance for the local processes. This involves the establishment of policies and principles that take into account the national culture, while having an eye to harmonization of key principles with other national authorities (Gauthier and Griffin, 2005). The requirements to ensure the effective functioning of ACCs as integrated and accountable parts of national oversight systems, and as keystones of international harmonization, are:

- the evaluation of the efficiency of ACCs and the regular review of the guidance on the Terms of Reference for ACCs by the national regulatory organization;
- the provision of adequate support for the ACC by institutional administrators;
- mandatory theoretical and practical training of all animal users in the ethics of animal experimentation;
- the development of training manuals tailored for community representatives on ACCs;
- the provision of continuing education to members of ACCs through workshops and distance education; and
- facilitated and timely communications between chairs of ACCs nationally and internationally as needed.

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