

Impact of harmonization at the international level

G Demers

International Council for Laboratory Animal Science (ICLAS), Canadian Council on Animal Care, 365 Maricourt, St-Hilaire, QC, Canada J3H 4W1
Email: gdemers@ccac.ca

Abstract

With the globalization of research, and the recognition that different animal care and use standards exist around the world, the International Council for Laboratory Animal Science (ICLAS) identified a need for the harmonization of animal care and use guidelines worldwide. Since 2004, ICLAS has held International Meetings for Harmonization of Guidelines and invited representatives of national and international organizations that produce or use guidelines for the use of animals in science to participate in these meetings. This ICLAS initiative and its impacts at the international level will be examined.

Keywords: Animal welfare, guidelines, international harmonization

Various mechanisms for the governance of animal care and use exist worldwide, from the European Union's legislation-based system, to Canada's peer review, non-legislated oversight, to the United States' combination of legislated and non-legislated oversight. Given the global nature of science, this range of systems and differences in standards of animal care and use in different countries can make scientific collaboration between countries difficult and complicate the global acceptance of research data.

Furthermore, developing countries lacking an established mechanism for the governance of animal care and use can become overwhelmed by the range of governance systems available and discouraged from participating in international collaborations. Without internationally established and accepted guidelines for animal care and use, there is a concern that animal-based studies may be moved to countries with less stringent standards.

The International Council for Laboratory Animal Science (ICLAS) is an international non-governmental and non-profit scientific organization that exists to promote high standards of animal care and use in education, research, testing and diagnosis, to promote good science and foster humane practices in scientific research. Two of ICLAS's aims have led to the focus on the harmonization of guidelines:

- (1) ICLAS should promote worldwide harmonization in the care and use of laboratory animals;
- (2) ICLAS should promote the humane use of animals in research through recognition of ethical principles and scientific responsibilities.

Since 2000, ICLAS has developed practical initiatives to bring members of the international community together to

identify and recommend acceptance of suitable animal care and use guidelines as International Reference Documents. ICLAS's focus on harmonization of guidelines for animal use in research, teaching, testing and diagnosis is also based on a need that was identified by the Council for International Organizations of Medical Sciences (CIOMS) in its *International Guiding Principles for Biomedical Research Involving Animals* statement:

'Because of differing legal systems and cultural backgrounds there are varying approaches to the use of animals for research, testing, or training in different countries. Nonetheless, their use should be always in accord with humane practices. The varying approaches in different countries to the use of animals for biomedical purposes, and the lack of relevant legislation or of formal self-regulatory mechanisms in some, **point to the need for international guiding principles elaborated as a result of international and interdisciplinary consultations**'.¹

ICLAS supports the harmonization of existing national and international animal care and use policies, guidelines and other forms of regulation, as a reflection of the globalization of research. This does not mean standardization, as ICLAS considers that each country should be able to maintain an animal welfare oversight system that reflects its cultures, traditions, religions, laws and regulations. Harmonization allows countries to retain their unique oversight mechanisms, while encouraging the development of general principles and best practices with animals that all ICLAS member organizations agree upon and follow.

As an international umbrella organization, ICLAS is well suited to facilitate the harmonization of existing guidelines

for the use of animals in research, teaching, testing and diagnosis worldwide. Representatives of the principal organizations in the world that produce or use guidelines for the use of animals in research are invited by ICLAS to its International Meetings for the Harmonization of Guidelines. These meetings have been held on a regular basis since 2004, in conjunction with national and international meetings.

First International ICLAS Meeting for Harmonization of Guidelines (FELASA – Nantes, France, 2004)

The objective of this first meeting was to initiate dialogue on the harmonization of a number of published guidelines on animal use in science, with a view to reaching a consensus on the recognition of these guidelines at the international level. An ICLAS Working Group on Harmonization of Guidelines, composed of members of key organizations producing and/or using guidelines for the use of animals in research, was established during this meeting for this work, and this group continues to meet every 18 months.

Guidelines on euthanasia and humane research endpoints for animals were selected for evaluation and two ICLAS *ad hoc* subcommittees were formed to evaluate these guidelines, with the goal of identifying general principles. Following evaluation and discussion of both sets of guidelines, each subcommittee prepared a report, recommending to the ICLAS Working Group on Harmonization of Guidelines guidelines to be accepted as International Reference Documents. Following acceptance of the guidelines by the ICLAS Working Group, the documents were ratified by the ICLAS Governing Board.

Important outcomes of this first meeting include:

- The acceptance of two guidelines on euthanasia as International Reference Documents: the *2000 Report of the AVMA Panel on Euthanasia*² and the *Recommendations for euthanasia of experimental animals: Parts 1 and 2*.^{3,4} This last document is the report of the Working Party that was prepared for DGXI of the European Commission to be used with Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes (No L 358, ISSN 0378-6978, February 1996).
- The acceptance of two guidelines on endpoints as International Reference Documents: the *CCAC Guidelines on: Choosing an Appropriate Endpoint in Experiments Using Animals for Research, Teaching and Testing*⁵ and the *Guidance Document on the Recognition, Assessment, and Use of Clinical Signs as Humane Endpoints for Experimental Animals Used in Safety Evaluation*.⁶
- The publication of the results of the First International ICLAS Meeting for Harmonization of Guidelines in the paper *Harmonization of animal care and use guidance* in the journal *Science* in May 2006.⁷ In this publication, international principles for the establishment of humane endpoints and for animal euthanasia are identified.

Second International ICLAS Meeting for Harmonization of Guidelines (AALAS – St Louis, USA, 2005)

The globalization of research and the movement of scientists around the world have created a need to evaluate guidelines on animal user training programmes already in place in different countries or regions of the world. The goal of this evaluation was to identify a core component in training guidelines from the United States, Europe and Canada. The importance of national or regional requirements was also highlighted.

Because most developing countries do not have a formal programme in place for the ethical review of animal care and use practices in science, scientific organizations in these countries are faced with a lack of guidance for the implementation of processes to encourage appropriate animal care and use. Policy documents and guidelines from the United States, Europe and Canada on the topic of ethical review of animal care and use were discussed.

Following this meeting, each ICLAS subcommittee prepared a preliminary report on their specific topic. These documents were revised and refined by the ICLAS Working Group on Harmonization of Guidelines during the Third International ICLAS Meeting for Harmonization of Guidelines in Italy, in June 2007. Final documents are expected to be completed and published in 2008.

Third International ICLAS Meeting for Harmonization of Guidelines (FELASA – Cernobbio, Italy, 2007)

In addition to the work already described, the ICLAS Working Group on Harmonization of Guidelines initiated the evaluation of new and existing guidelines related to genetically-engineered animals. Documents from Australia, the United Kingdom, the United States and Canada were discussed.

An ICLAS *ad hoc* subcommittee was created and this subcommittee will prepare a preliminary report for the next meeting of the ICLAS Working Group on Harmonization, which will take place in Indianapolis, USA, in November 2008.

Impact of harmonization at the international level

Since 2004, ICLAS has played an important role in the recognition of animal care and use guidelines as International Reference Documents. The positive impacts of this ICLAS initiative are detailed below.

Developing countries

Through its harmonization initiative, ICLAS will provide guidance to scientific organizations around the world in the area of implementation of ethical review processes.

Scientific journals

ICLAS hopes to encourage all scientific journals to require all research to have received ethical review prior to commencement of the research. Scientific journals will also be encouraged to adopt the internationally accepted guidelines on euthanasia and endpoints when evaluating scientific manuscripts.

Scientists

The harmonization of guidelines on animal user training programmes will facilitate the movement of scientists, and collaborations between institutions, around the world. The importance of having good training programmes in place for animal users has been highlighted, and this will facilitate the implementation of good animal practices worldwide.

Animals

Harmonization of animal care and use guidance is leading to the implementation of improved animal practices worldwide.

The meetings on harmonization of guidelines have served to maintain a dialogue on good animal practices and on animal welfare between key scientific organizations, including the Canadian Council on Animal Care (CCAC, Canada), the Institute for Laboratory Animal Research (ILAR, USA), the World Organisation for Animal Health (OIE, France), the Federation of European Laboratory Animal Science Associations (FELASA), the International Association of Colleges of Laboratory Animal Medicine (IACLAM) and several national laboratory animal science and medicine organizations.

Collaborations in animal-based research

The harmonization of animal care and use guidance has provided an opportunity to highlight the importance of data sharing to avoid duplication of research and to reduce the numbers of animals used in research. The importance of maintaining dialogue between regulatory bodies was also highlighted.

ILAR-ICLAS

Parallel to the ICLAS initiative on harmonization, ILAR has initiated its own process to develop science-based guidelines through international workshops. ICLAS has co-sponsored this work and participated in the workshops held in 2003, 2004 and 2005.

ICLAS meetings

ICLAS has created opportunities for key scientific organizations to meet, share and exchange information on a regular basis:

- ICLAS International Meetings for Harmonization of Guidelines, which are held every 18 months;
- ICLAS Consortium Meetings, where laboratory animal science organizations are invited to discuss their activities, are held annually.
- ICLAS International Meetings are held for specific purposes, as needed:
 - ICLAS-CCAC: 2001;
 - ICLAS-OIE: 2006.

COSPAR-ICLAS

The Committee on Space Research (COSPAR) is in the process of developing guidelines with respect to the use of animals in space research. Potential collaboration with ICLAS was highlighted in COSPAR's draft document.

OIE-ICLAS Agreement

Ongoing interaction and communication with the OIE has led to an agreement between both organizations on the development of an OIE-ICLAS Agreement. The main elements of this agreement include the promotion of high standards of animal care and use in education, research, testing and diagnostic work, cooperation in the development and revision of international animal welfare standards and guidelines relevant for both organizations, and the role and responsibilities of the veterinary profession in the welfare of animals used in experimental work. This agreement was scheduled to be ratified in December 2007 at the OIE headquarters in Paris, France.

CIOMS-ICLAS

As an Associate Member of the CIOMS, ICLAS has been invited to participate in the CIOMS Executive Committee and General Assembly meetings in December 2007.

Conclusions

The harmonization of existing guidelines for the use of animals in science is essential in the context of the globalization of research. ICLAS, as an international umbrella organization, should continue to play its role of facilitator in this area. To ensure the continuity of this important ICLAS initiative, human resources and additional funding will be needed.

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