

**International Harmonization of Guidelines on
the Ethical Review of Proposals to Use Animals in Science**

“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

There are institutional, local, national and international mechanisms that regulate animal use in science, in addition to other obligations for scientists who plan to use animals. These include requirements related to standards of animal care and ethical animal use established by institutions, agencies, organizations and government departments that fund and undertake animal-based science, as well as the requirements for meeting specific standards of animal care and use laid down by many international and national scientific journals.

Most processes for overseeing animal use in science emphasize the tenet of the Three Rs² of replacement, reduction and refinement of animal use. There is a variety of mechanisms in place to ensure that the Three Rs and other ethical principles have been considered for each project involving animal use. Some countries use local or institutional committees also known as ethics committees³, some use national ethical

¹ International Guiding Principles for Biomedical Research Involving Animals (1985), Committee of International Organizations of Medical Science (CIOMS).

² The principles of the Three Rs – Replacement, Reduction and Refinement were first enunciated by the UFAW research scholars WMS Russell and RL Burch in 1959 and form the basis for most national systems of oversight of animal use in science.

³ Ethics committees are referred to by a variety of titles in various countries: for example, institutional animal care and use committees (US), animal ethics committees (New Zealand and Australia), animal care

review processes, some use regional processes, and some work through individuals (officers, officials, inspectors) designated with responsibility for ethical oversight. In many countries, the ethical review process involves several of these different approaches.

As reported in *Science* in 2006⁴, “The patchwork of mechanisms can be especially daunting for developing countries, in elaborating their own mechanisms and in international collaboration”. The International Council for Laboratory Animal Science (ICLAS) is therefore actively pursuing its work to “identify solid, practical guidance that can easily be used by the international community to promote good animal welfare while conducting sound animal-based science”.

In this spirit, on November 6, 2005, the ICLAS Working Group on Harmonization met in Saint-Louis, Missouri (US), to examine national/regional guidelines on the ethical review of proposals to use animals in science and to make recommendations for adoption of guidelines on ethical review for international recognition.

The ICLAS Working Group agreed on general principles for ethical review of animal-based studies that are already part of most systems, and that should be considered no matter what the exact nature of the review process. It recommends three documents as suitable for use as international references, namely the:

- Applied Research Ethics National Association (ARENA)/US Office of Laboratory Animal Welfare (OLAW) *Institutional Animal Care and Use Committee Guidebook* (2002), including in particular Section C – Review of Proposals (pp. 83-156) of this document;
- Canadian Council on Animal Care (CCAC) *guidelines on: animal use protocol review* (1997);
- Principles and Practice in Ethical Review of Animal Experiments across Europe: A report of the Federation of European Laboratory Animal Science Associations

committees (Canada), institutional animal ethics committees (India), animal research ethical committees (Brazil), internal committees (Israel) and local review committees (Thailand).

⁴ Harmonization of animal care and use guidance, G. Demers, G. Griffin, G. De Vroey, J.R. Haywood, J. Zurlo, M. Bédard, *Science*, vol. 312:700-701, 5 May 2006).

(FELASA) Working Group on Ethical Evaluation of Animal Experiments. Smith, J.A., van den Broek, F.A.R., Martorell, J Cantó, Hackbarth, H., Ruksenas, O., Zeller, W., December 2005. A summary version of this report was published in *Laboratory Animals*, Volume 41, Number 2, April 2007, pp. 143-160.

These references provide general guidance on ethical review of proposed animal use in science that is suitable for local or institutional committees, but whose principles can also be extended to regional and national processes. They are all based on the general principles included in Section B of this document. The Canadian and US documents are best suited to systems where institutional committees occupy an important place and responsibility is largely devolved to the local level. The FELASA report details thirty overarching principles for an ethical review process. The US document, in particular Section C, describes legal requirements in the US and, like the Canadian and European documents, also describes fundamental elements that should be included in the ethical review of proposed animal use.

The ICLAS Working Group recognizes that there are many other sources of guidance and information on ethical review of animal experiments, some of which are listed in Section D of this document.

The following overarching principles are intended to provide guidance to countries that do not yet have ethical review processes for proposed animal use in science, as well as to those countries, regions, organizations and institutions that may wish to refine their existing processes.

B. General Principles

1. Whenever possible, methods employed to achieve scientific objectives should avoid the use of animals.
2. Where animal use is unavoidable, the proposed project should have been demonstrated to have merit, in terms of its potential to advance scientific knowledge and/or benefit human or animal health (scientific merit), to protect/benefit humans, animals and/or the environment with respect to new products/devices or to toxic substances (regulatory testing) or to teach animal-based principles and procedures (pedagogical merit).
3. The expected benefits to humans, animals or the environment of the proposed project involving live animals, should be weighed against the likely harms done to the animals, and opportunities should be sought to maximize benefits and minimize harms.
4. The species/strain (model) and numbers of animals to be used should be scientifically justified to use optimal numbers of animals (neither too many nor too few). The experimental design should be optimized according to the type of study undertaken.
5. Studies should be designed to refine procedures undertaken on animals to the greatest extent possible, and standards of care and housing of animals should be optimized by those responsible for them.
6. Pain or distress likely to be experienced by the animals must be prevented, or at least minimized, with veterinary advice, for example through appropriate anesthesia, analgesia and/or other measures as applicable to the type of animal and study.
7. Those who use or care for animals must be skilled and competent to do so, both for their own safety and for the health and welfare of the animals (see *International Harmonization of Guidelines on Training*, ICLAS 2008 (in preparation)).
8. The earliest possible endpoint for the animals should be used consistent with the scientific objectives of the study (see *International Harmonization of Guidelines on Humane Endpoints*, ICLAS 2005).

9. A method of euthanasia that is appropriate for the species, life stage and type of work should be chosen (see *International Harmonization of Guidelines on Euthanasia*, ICLAS 2004).
10. There should be a mechanism to ensure initial and ongoing review of the work and to use the results of the work to inform future scientific and ethical reviews.

C. International Reference Documents

The ICLAS working group on harmonization fully supports the use of the following documents as international references.

- Applied Research Ethics National Association (ARENA)/Office of Laboratory Animal Welfare (OLAW) *Institutional Animal Care and Use Committee Guidebook* (2002), including in particular Section C – Review of Proposals (pp. 83-156) of this document, <ftp://ftp.grants.nih.gov/IACUC/GuideBook.pdf>
- Canadian Council on Animal Care (CCAC) *guidelines on: animal use protocol review* (1997),
http://www.ccac.ca/en/CCAC_Programs/Guidelines_Policies/GDLINES/PROTOCOL/PROTGDE.HTM
- Principles and Practice in Ethical Review of Animal Experiments across Europe: A report of the Federation of European Laboratory Animal Science Associations (FELASA) Working Group on Ethical Evaluation of Animal Experiments (2005) http://www.felasa.eu/Documents/Workinggroups/final_reports/WG_ethical_review.pdf
f . Summary report published in *Laboratory Animals* (2007), Volume 41, Number 2, April 2007, pp. 143-160, <http://www.lal.org.uk/pdffiles/felasaethics.pdf>

D. Additional References

These references are provided to offer further guidance in ethical review of proposed animal use.

- Australian Government National Health and Medical Research Council (2004). Australian code of practice for the care and use of animals in scientific procedures. Australian Government, <http://www.nhmrc.gov.au/publications/synopses/eal6syn.htm>
- Canadian Council on Animal Care (2006). CCAC policy statement on: terms of reference for animal care committees. CCAC, Ottawa, http://www.ccac.ca/en/CCAC_Programs/Guidelines_Policies/POLICIES/TERMS00E.HTM
- Jennings, M. and Miller, J. (2000). Harmonising IACUC practices, pp. 1705-11, in : Progress in reduction, refinement and replacement of animal experimentation (Balls, M., van Zeller, A.M., Halder, M.E. eds). Elsevier Science BV: The Netherlands.
- New Zealand National Animal Ethics Advisory Committee (2002). Good practice guide for the use of animals in research, testing and teaching. MAF: Wellington, <http://www.biosecurity.govt.nz/animal-welfare/naeac/papers/guide-for-animals-use.htm>
- Science Council of Japan (2006). Guidelines for Proper Conduct of Animal Experiments, <http://www.scj.go.jp/ja/info/kohyo/pdf/kohyo-20-k16-2e.pdf>
- UK Animal Procedures Committee (2003). Review of cost-benefit assessment in the use of animals in research, <http://www.apc.gov.uk/reference/costbenefit.pdf>
- US Public Health Service Policy on Humane Care and Use of Laboratory Animals (2002), <http://grants.nih.gov/grants/olaw/references/PHSPolicyLabAnimals.pdf>
- US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training, 1985, <http://www.absc.usgs.gov/research/vet/policies/IRACPRIN.htm>