Harmonization of Animal Care and Use Guidance

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Societal expectations for improvements in the health of humans and animals require scientific studies involving the use of animals. At the same time, the public is concerned about the welfare of animals used in science. Animal welfare is also of importance because of the link between healthy, well-cared-for animals and sound science. Most national oversight mechanisms emphasize basic principles of humane science, in particular the “three R’s” (replacement, reduction, and refinement of animal use). However, the oversight of animal care and use occurs through a wide variety of local, national, and international mechanisms, some based on legislation (the European Union (EU); (2)), others on peer review or other forms of nonlegislated oversight (Canada) and yet others on a combination of legislated and nonlegislated oversight (United States). This patchwork of mechanisms can cause problems, given the global nature of science.

Different standards for animal care and use can complicate the comparison of results from animal-based studies and the reproducibility of such results and can also slow international scientific collaboration. For example, CO2 euthanasia is more commonly used for rodents in the United States than in the EU, and T-61 (a combination of three drugs—a local anesthetic, a general anesthetic, and a curariform drug) is available to animal users in Europe but not the United States. There are also international trade implications: multinational companies face the challenge of having to work with research and testing sites operating within very different regulatory structures. Specific standards of animal care and use required by scientific journals can also present a barrier to publication. The patchwork of mechanisms can be especially daunting for developing countries, in elaborating their own mechanisms and in international collaboration. Finally, there is concern that differences in animal care and use requirements may lead to the transfer of animal-based studies to countries with weaker requirements. As far back as 1985, the Committee of International Organizations of Medical Science (CIOMS), which works closely with the World Health Organization, said “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” (3).

There are international efforts to use guidance that is based on performance standards [i.e., standards that define an outcome and provide criteria for assessing that outcome, but do not limit the methods by which that outcome may be achieved (4)], and to work on filling gaps in the science needed for sound animal welfare guidance. Examples of international collaboration include the CIOMS Principles, the Mutual Acceptance of Data Program of the Organisation for Economic Cooperation and Development (OECD), and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). These instances of collaboration have reduced unnecessary duplication of studies involving animals by developing internationally accepted common methods for chemical testing and drug development.

Guidance on the recognition of clinical signs as humane end points is now being implemented by member nations of the OECD, in conjunction with the OECD test guidelines for safety evaluation, which means that regulatory agencies in these countries should no longer require death in extremis as an end point for safety tests (5). In countries that are not OECD members, death may still be commonly accepted as an end point.

The International Council for Laboratory Animal Science (ICLAS (6)) has brought members of the

**Principles for Establishment of Humane End Points**

1. There is strong evidence that animals experience pain and distress in situations comparable to those that cause pain and distress for humans.

2. Death or severe pain and distress should be avoided as end points.

3. The earliest possible end point should be used that is consistent with the scientific objectives.

4. Studies should be designed to minimize any pain or distress likely to be experienced by the animals, while meeting the scientific objectives.

5. The duration of studies involving pain and distress should be kept to a minimum.

6. Pilot studies should be encouraged as a means of determining morbidity, time course of effects, and frequency of observations required to set an earlier end point.

7. Before commencing the experiment, agreement should be reached on (i) appropriate end points for the study and (ii) the person or persons to be responsible for making the judgment that the end point has been reached.

8. A team approach should be used, employing the professional judgment of the scientist, veterinarian, animal care staff, and ethics committee to agree on the appropriate end point for the study.

9. Research and animal care staff must be adequately trained and competent in recognition of species-specific behavior and, in particular, species-specific signs of pain, distress, and moribundity.

10. Animals should be monitored by means of behavioral, physiological, and/or clinical signs at an appropriate frequency to permit timely termination of the experiment once the end point has been reached.

International guidance for animal care and use is important to facilitate conduct of appropriate animal-based science on a global level and to protect the welfare of animals used in science.

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ICLAS will continue to work with its many partners around the world 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.

References and Notes


6. International Council for Laboratory Animal Science (ICLAS) ([www.iclas.org](http://www.iclas.org)).


8. Canadian Council on Animal Care (CCAC), "[CCAC guidelines on: choosing an appropriate endpoint in experiments using animals for research, teaching, and testing]" (CCAC, Ottawa, 1998);


11. List of participants available on Science Online.


15. ICLAS, "International harmonization of guidelines on euthanasia" (ICLAS, Nantes, France, 2004), approved in Buenos Aires, Argentina, November 2004, available on Science Online.

16. ICLAS thanks all those who have volunteered their time and expertise for its work, in particular those working on international harmonization.

Supporting Online Material

www.sciencemag.org/cgi/content/full/312/5774/700/DC1

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