REPORTS AND COMMENTS

Humane endpoints for animals used in safety evaluation

The Organisation for Economic Co-operation and Development (OECD) set up an *ad hoc* working group in 1994 to develop guidelines on when laboratory animals used in toxicity testing should be euthanased for humane reasons. The efforts of this working group came to fruition with the publication of a Guidance Document (see details below) in November 2000.

The aim of the application of humane endpoints to toxicological studies is the accurate prediction of severe pain, severe distress, suffering, or impending death, before it occurs. These guidelines discuss the recognition and assessment of pain, distress and suffering through frequent and careful observation and the recording of signs including changes in external physical appearance, behavioural abnormalities, and measurable clinical parameters (body temperature, haematology etc). Signs indicative of impending death and of severe pain and distress are stated, and clinical signs and conditions indicating the need for closer observation or humane killing are listed alphabetically and briefly outlined in an appendix. References are given to sources of information on methods of humane killing. The document also provides guidance on the humane conduct of specific types of toxicity testing, including acute single dose studies, ocular irritation studies, systemic repeated-dose studies, reproductive toxicity studies, sensitisation studies, and chronic toxicity and carcinogenicity studies.

This is an important publication. The principles and approaches it outlines should be applied as fully as possible to minimise or prevent suffering of animals used in toxicity studies.

Guidance Document on the Recognition, Assessment, and Use of Clinical Signs as Humane Endpoints for Experimental Animals Used in Safety Evaluation (November 2000). OECD Environmental Health and Safety Publications Series on Testing and Assessment No. 19. 38 pp. A4 paperback. Published by the Environment Directorate, Organisation for Economic Co-operation and Development, Paris. Available from OECD, 2 rue André-Pascal, 75775 Paris CEDEX 16, France. Electronic copies are available free of charge at http://www.oecd.org/ehs/test.

Recommendations on methods for euthanasia

In 1999, the Executive Board of the American Veterinary Medicine Association convened a panel to update and revise the AVMA's information and recommendations on euthanasia. The report of this 16-person panel has now been published in the March 2001 edition of the *Journal of the Veterinary Medicine Association* (see details below). The report, which is intended for use by members of the veterinary profession, covers euthanasia of animals in research and animal care and control facilities, and also includes information on horses and wildlife. It is noted that those responsible for euthanasia of healthy animals must be cognisant of professional and societal ethical concerns, but these subjects were judged to be outside the scope of the report and are not discussed. The 26-page paper focuses largely on the technical aspects.

The introductory sections include: general considerations, in which a brief outline of the panel's criteria for evaluating methods of euthanasia is provided; animal behavioural considerations, on how to recognise and avoid causing fear and other unpleasant emotional states; and human behavioural considerations, on the potential adverse emotional impacts on humans involved in animal euthanasia. The following sections include reviews of inhalant agents, non-inhalant pharmaceutical agents, physical methods and special considerations for euthanasia of horses, of animals intended for human consumption, and of zoo, wild, aquatic and ectothermic animals. Four appendices list: (i) acceptable agents and methods; (ii) the modes of actions of these acceptable methods and agents; (iii) conditionally acceptable agents and their modes of action; and (iv) some unacceptable agents and methods.

Although 215 publications are cited in the report, surprisingly these did not include the comprehensive review papers by Close and others[1,2] based on the Report of the Working Party on euthanasia prepared for DGXI of the European Commission. This seems a strange oversight. There are differences between what is judged acceptable on the east and west sides of the Atlantic. For example, the AVMA panel concludes that neuromuscular blocking agents may be used for restraint if immediately prior to the use of some acceptable form of euthanasia and under other, albeit strictly limited, circumstances. Some discussion about the differences in the stances adopted by other groups (such as the above-mentioned European Group) and on the reasons for these would have strengthened the document. However, it is a valuable review, particularly as the recommendations are in line with relevant USA laws and guidelines, for use in the USA.

2000 Report of the AVMA Panel on Euthanasia (March 2001). *Journal of the American Veterinary Medicine Society 218*: 669-696

[1] **Close B, Banister K, Baumans V, Bernoth E-M, Bromage N, Bunyan J, Erhardt W, Flecknell P, Gregory N, Hackbarth H, Morton D and Warwick C** 1996 Recommendations for euthanasia of experimental animals. Part 1. *Laboratory Animals 30*: 293-316

[2] **Close B, Banister K, Baumans V, Bernoth E-M, Bromage N, Bunyan J, Erhardt W, Flecknell P, Gregory N, Hackbarth H, Morton D and Warwick C** 1997 Recommendations for euthanasia of experimental animals. Part 2. *Laboratory Animals 31*: 1-32

Consistency of judgements on animal research protocols

At most research institutions in the USA, studies involving animal use have to be approved by the Institutional Animal Care and Use Committee (IACUC). A similar system is operated in many other countries including, for example, Australia and New Zealand. In the UK, although responsibility for approval of the use of animals in research resides with the Home Office, the role of the local ethical review process (ERP) corresponds quite closely to that of IACUCs. Several federal and professional guidelines require IACUCs to consider aspects such as the value of the proposed research at fundamental and applied levels, the quality of the research design, the justification for the type and number of animals to be used, and the degree of pain and stress to the animals involved. Cost–benefit assessment (weighing the adverse welfare impacts on the animals involved against the potential benefits of the research) undertaken in some collective way (eg by IACUC or ERP), rather than by one individual, is believed by many to be crucial for reaching ethically sound conclusions. There is perhaps a general assumption also that there is a 'right' answer to be found and that properly functioning ethical review committees (including IACUCs) will, at least for the most part, find this right answer. It would be comforting to know that such committees tend to reach the same conclusions about the same proposals — rejecting all those in which the costs appear disproportionate to the benefits and approving only those in which the benefits clearly outweigh the costs and in which the costs are limited. The results of a recent study do not provide this comfort.

Plous and Herzog (2001) asked 50 IACUCs to submit their three most recently reviewed research protocols in animal behaviour, and distributed each of these among the IACUCs for review a second time, so that each protocol was reviewed independently by two IACUCs. The IACUCs were asked to recommend one of four possible judgements: approve as written, approve with conditions, defer decision pending further information, or reject. They found that the judgements of the committees were not significantly correlated. Furthermore, it was found that, regardless of the degree of severity of the procedures involved in the protocols, inter-committee agreement did not exceed chance levels.