

## Summary of the workshops

During the Conference three parallel workshops were held on 'Humane endpoints in toxicity testing and cancer research' (chaired by Dr Jon Richmond, Home Office, UK), 'Humane endpoints in infection models and vaccine quality control' (chaired by Professor Jann Hau, University of Uppsala, Sweden), and on 'Humane endpoints, test regulations, animal welfare regulations and training' (chaired by Dr Paul de Greeve, Ministry of Public Health, Welfare & Sports, The Netherlands). This document represents the edited reports of the workshops.

### General

Justification is the key to ensuring that relevant, sound, refined animal use is the norm (both the science and the welfare issues require this) – and that public confidence and support are maintained. The need to justify why animal work is done, how it is done and the endpoints applied were acknowledged. In the context of the workshops, justification is required at three levels as follows.

1. The regulatory requirements and research objectives need to be justified; not just by stating what is required, but by explaining why it is required. Regulatory authorities and scientists have to explain what they want to do and why.
2. Having justified the need for work to be undertaken, the study designs to be used need to be verified, validated and justified. There was a strong feeling that regulators should signal that they expect alternative protocols to be applied whenever possible.
3. The endpoints to be applied in any study need to be specifically justified, especially when they cause animals to suffer.

### Key principles for best practice

There is agreement that one of the objectives for best practice is to minimize animal suffering. To this end validated methods not requiring animal use are to be preferred to the use of animals and, when animals are used, early endpoints are to be preferred to endpoints indicative of animal suffering such as morbidity or mortality. Death should seldom if ever be set as an endpoint. It was felt that some test requirements were difficult to justify and that only well-justified studies

with well-defined objectives could be defended.

It is important that attention is drawn to published guidance, and that such material is readily available, e.g. databases could be set up and CD-ROMs produced. Not only must guidance be kept up-to-date, it must also be concise and written in such a way that it can be understood by all those involved in the studies. The illustration of key points by using practical examples would be useful. Moreover, it was felt that best practice needs to be better publicized.

It is important that appropriate evidence-based 'situational' endpoints are determined before work starts and are applied promptly, and that a range of relevant welfare and scientific expertise is employed to determine these early endpoints. Staff training and appropriate observation schedules are essential, as are good teamwork and communication. The importance of pilot studies and the use of tiered (hierarchical) approaches were stressed in the workshops.

It was strongly felt that animals found dead represented missed opportunities for refinement, and also risked the loss of valuable experimental data. Thus deaths may represent both unnecessary suffering and bad science.

Uniform means of describing common events and clear agreement about what constitutes 'impending death', 'moribund' and 'severe pain' and 'severe distress' would improve both science and animal welfare.

### Obstacles to implementing best practice

#### *Scientific*

It was felt that scientific objectives and some of the test requirements were not always

well-defined, and that the scientific relevance of some regulatory requirements could be questioned. There is a need to support the development of validated humane endpoints through the provision of resources such as staff time and money.

### *Regulatory acceptance*

Until there is true global harmonization of test requirements, the acceptance of refined endpoints in one country will have little impact on other countries. It was acknowledged that the time taken to move from scientific validation to regulatory acceptance of more refined methods slowed the rate of progress. It was conceded, and regretted, that the largely traditional nature of some of the routine animal-based tests actually hindered the validation of better mechanistic alternatives. Changes to research methods may cause problems in benchmarking data against previous data-sets or the ongoing work of others. Consequently, inertia and custom and practice slow progress until it becomes clear that regulators and the scientific community are prepared to accept data generated using more refined methods.

### *Resources*

New technologies can initially be costly in terms of equipment, staff and training, and may require additional work to introduce and validate the new refined methods. It can also increase the documentation requirements. The Conference presentations contained practical examples where the economic, time and staff resource implications relegated some means of identifying and implementing the most refined endpoints to research tools, rather than promoting them into everyday practice.

### *Other*

- There can be a reluctance on the part of regulatory authorities to explain and justify what they expect or do.
- It may be difficult to determine what is current best practice and what opportunities there are to move towards more humane endpoints.

- National control over animal use may be slow to push for the most refined methods.
- In some instances more refined endpoints may require more animals to be used even if the total suffering is reduced.

### **Factors promoting best practice**

Notwithstanding public opinion, there are reasons why all stakeholders should be pushing for more refined endpoints and hence better science.

- No-one sets out to cause, or likes to be accused of causing, unnecessary and avoidable suffering to animals.
- Regulatory authorities and research scientists require the most relevant data to inform their decisions. Animal studies are costly, and to some extent are empirical rather than clearly derived from understanding of mechanisms.
- The public want safer products, better health-care, and at the same time no more animal testing or suffering than is absolutely necessary.

### **Training programmes for animal caretakers, technicians and scientists**

Several major limitations in training programmes with respect to humane endpoints were identified.

- The lack of validated information about earlier endpoints.
- The limited number of specific and even general 'pain' scoring systems that can be easily used.
- The lack of consistency of training programmes from one institution, or country, to another.
- The need for improved hands-on training. Additional opportunities should be provided at institutions for hands-on training tailored specifically to that institution's research projects, particularly in clinical observation skills. Since severe clinical signs may be observed only rarely, it is important that personnel be trained not only in the signs of impending death, but

also in the signs that indicate an animal is unlikely to die. Because of the rarity of some clinical signs, and because there are ethical issues associated with the use of animals for such training, videos and CD-ROMs can be useful adjuncts in hands-on training programmes.

- There is a lack of development of: (a) more specific training recommendations; (b) supplemental course materials for training needs in specific situations; (c) a list of video and CD-ROM resources; and (d) written material on methods for assessing humane endpoints, including the use of better monitoring techniques like temperature and activity transponders. FELASA should be approached about developing these recommendations and materials.
- The frequent failure to develop mandatory qualifications at a national level for animal care staff, and promote harmonization of these standards among different countries. EFAT (the European Federation of Animal Technologists) is presently developing a training booklet intended to harmonize standards.
- Although the provision of training is mandated in most countries, there may be no requirement to attain a certain level of competence (e.g. certification). The training of scientists has lagged behind training of animal care staff. Professional organizations could help in this respect, e.g. Eurotox trains toxicologists for registration, but their training programme could also include training on assessment of clinical signs and humane endpoints.
- The lack of standardized methods for assessing the outcome of training programmes (i.e. competence of those trained).

## Recommendations on best practice

1. Best practice should be identified and promulgated and information has to be constantly updated.
2. The pace of regulatory acceptance should be quicker and more responsive so as not to obstruct the effective implementation of more humane endpoints.
3. Scientists and regulators must justify test requirements, study design and endpoints. The lack of harmonized test requirements between countries should be eliminated.
4. The existing texts on humane killing on welfare grounds would be better implemented if the signs indicative of 'impending death, moribund, severe pain and severe distress' were agreed and documented in detail for use. This should be a priority for Regulatory Authorities
5. More research funds and other resources should be directed towards the development of humane endpoints.

## Recommendations on training

6. Improve hands-on training.
7. Develop training recommendations and materials.
8. Encourage the development of mandatory qualifications on a national level for animal care staff, and promote harmonization of these standards among different countries.
9. Develop more formal training programmes for scientists.