

Mr Harald Schmidt
Nuffield Council on Bioethics
28 Bedford Square
London
WC1B 3JS

tel +44 020 7451 2591
fax +44 020 7451 2692
www.royalsoc.ac.uk

18 December 2003

Policy no: 29/03

Dear Mr Schmidt

Nuffield Council on Bioethics consultation on the ethics of research involving animals

Please find enclosed the Royal Society's response to your consultation, which has been produced during my time as Chairman of the Royal Society Animals in Research Committee and Vice-President of the Royal Society, in consultation with members of the Committee. The Royal Society takes an active role in policy discussions on the use of animals in research, and we welcome the invitation to engage in a discussion on the ethical issues raised by research involving animals.

Along with the great majority of the scientific community and the wider public, the Royal Society considers that the benefits from the use of animals in research provide the justification for the research that led to them. Such research must be conducted in the knowledge that all possible measures have been taken to minimise the suffering of animals used in research. Thus the Royal Society strongly endorses the principle of the '3Rs', which are enshrined in UK legislation, in providing a robust but not restrictive legislative system that enables the continued development of scientific and medical advances through the use of animals in research.

Q1 What is your view about the use of animals in research?

The Royal Society has made a clear statement of its view on the use of animals in research (Annex 1). Both humans and animals have benefited immensely from the research involving animals, with virtually every medical achievement in the past century reliant on the use of animals in some way. Developments in the treatment of diabetes, asthma, leukaemia and heart surgery transplant procedures, amongst others, have been made possible through the use of animals in scientific research. The public increasingly accepts the use of animals in research, with a MORI poll conducted in 2002 finding that 90% of the public accepted the need for the use of animals in research, providing that certain conditions are met, which are: there is no unnecessary suffering; the research is for serious medical or life-saving purposes; and there is no reliable alternative to their use. At the same time, the Society also recognises that special ethical considerations are involved and that animal research must be undertaken only with the greatest care.

The validity of particular experiments on animals must be argued on a case-by-case basis, with each application to undertake research being subject to rigorous examination in the UK. Judgements about the potential value of an experiment would be affected by the aim of the study. One type of work involving animals is mandatory testing of new substances, which involves essential assessment of whether a chemical, new drug or vaccine, will be harmful to humans. The cost/benefit assessment for this work should, in theory, be reasonably straightforward in terms of assessing cost by the numbers and types of animals and the level of animal suffering against the beneficial outcome for medical understanding.

Cost/benefit assessments of other areas of work can be more difficult when the research involves understanding biological processes in humans or undertaking fundamental research that is exploratory and where the aim is to gain understanding of a biological system and generate hypotheses for further investigation. While the possible clinical benefits of such research cannot be assessed in advance, it is clear that much of this research has been essential to subsequent major advances in human and veterinary medicine. Traditional cost/benefit analysis of exploratory approaches poses problems because of the difficulty of putting a value on understanding or knowledge. In such situations the likelihood of valuable outcome will be judged in terms of the intrinsic interest of the problem, the quality of the proposed science and the track record of the investigator, rather than attempting to measure the specific research outcome.

Assessment of the scientific validity of a project proposal must take into account whether the problem to be addressed is important, whether the results of the experiments proposed are likely to provide new and important information, and whether this new information is likely to be useful for understanding basic biological processes and/or disease in both humans and animals. In terms of overall outcome, most referees will try to assess what the contribution to knowledge and understanding will be, and will also try to assess the likely medical, veterinary and social benefits that will accrue from the experiment, and balance these against likely levels of suffering.

Q2 What are your views about the use of genetically modified animals in research?

The Royal Society's position has been set out fully in the attached document (Annex 2), which concludes that a strong scientific case can be made for the use of genetically modified animals in order to understand human and animal disease. Although it is possible that certain applications of genetic modification are capable of generating special welfare problems, it is the Society's view that no qualitative distinction in terms of welfare that can be made between genetic modification using modern transgenic technology and modification produced by artificial selection or mutagens. Indeed, the targeted character of modern technology may provide fewer welfare problems and a faster route to improving welfare than older techniques. The assessment of acceptability should be based on cost/benefit considerations and should be independent of the manner in which any suffering is produced.

Applications for the use of transgenic animals include producing human proteins, replacing primates in testing polio vaccine, and developing disease resistance in target species. Most transgenic animals are currently being treated as exploratory models, and have made an enormous contribution to our understanding of many basic cellular processes. For example, large numbers of oncogenes and tumour suppressor genes have been identified and understood by the use of transgenic mice which either over-produce the protein or in which the gene function has been knocked out. However, the large number of unknowns and potential for surprises suggest that understanding of the control of cell multiplication and death is still far from perfect. For example, it was a surprise that the p53 knockout mouse develops normally to adulthood in view of the normal importance of this gene's product in development. In view of the large number of these molecules involved in essential processes and the complex interactions between them, it is difficult to think of a more effective research technique. The level of understanding achieved by use of these transgenic mice is already well advanced and it is hoped that this technique will lead to a greater knowledge of, and eventual cure for, many cancers.

Q3 What is your view about the alternatives

The Royal Society is fully supportive of current UK law, which requires that all possible measures must be taken to minimise the suffering of animals used in research. The guiding principles of animal welfare are the so-called '3Rs', refinement, reduction and replacement, which were first clearly defined in 1959. The Royal Society strongly endorses the principle of the '3Rs'. This means that every effort must be made:

- to **refine** the procedures so that the degree of suffering is kept to a minimum.
- to **reduce** the number of animals used in research to the minimum required for statistically meaningful results.
- to **replace** the use of live animals by non-animal alternatives.

Current UK legislation requires all researchers who propose to undertake laboratory or fieldwork involving animals to give full consideration to the 3Rs and to seek independent advice from a local ethics committee.

Both reduction and refinement are goals that experimenters implement in their daily routines since additional benefits can arise such as better design leading to more statistical power without increasing the number of animals used, and fewer animals improving cost effectiveness. On other hand, reduction must not be taken to the point where quantitative findings are statistically meaningless. Replacement is more difficult to achieve because of the unique insights provided by use of whole animals, such as the complex feedback systems that operate in an integrated fashion in humans and other animals. These can sometimes be successfully modelled using computer simulations or studied in isolation using cells in culture, but such modelling is always best carried out alongside experimental work as systems interactions are difficult to replicate in isolation. A more detailed discussion of this issue can be found in the Royal Society's document, 'The use of non-human animals in research: a guide for scientists' (2004), which we will send to you on its publication.

Q4 What is your view about ethical issues relating to the use of animals in research?

The Royal Society takes the view that scientists who work with animals should take moral responsibility for the good welfare of the animals which they use. The Society shares the dominant view about animal welfare, which is that the more complicated the animal, the higher the capacity for suffering. Assessment of suffering using a human-centred approach involves establishing whether the animal has anatomical, physiological and biochemical mechanisms correlated with such experiences in humans. The approach also raises the issue of whether the animal performs in similar ways to humans who are believed to be suffering. If these mechanisms are identified, then the level of suffering can be established, helping to ensure that suffering is kept to a minimum.

The Society believes that many, sometimes contradictory, positions underlie perceptions of the costs of using animals in scientific research. It is likely that many people hold at the same time many different beliefs about why animals should not be harmed. In order for ethical considerations to feature in cost-benefit analyses, it helps to know what cost is being talked about in any particular analysis. Deriving a 'balance' between cost and benefit is not easy at the best of times because the two are not measured in the same terms. Therefore, the metaphor of weighing one against the other is misleading if it is used in a precise sense. In practice, it is often used in the vaguer sense of comparing one outcome with another. This is an important point because decisions about the acceptability of the use of animals in research depend on independent value judgements of costs and benefits and cannot be derived by any precise methodology. For example, the vexed issue of genetic modification is regarded by some as unacceptable interference, or 'playing at God', and as a valuable advance in technology by others. It is doubtful whether any compromise can be found between the two groups holding such divergent views because of different starting positions of what constitutes a cost of doing research on animals and what is a benefit. It is the Royal Society's position that such an ethically contentious issue, as in stem cell research, can only be settled by Parliament. Until it has been, the Society believes that the most satisfactory approach to cost-benefit analysis is by establishing the ethical principles that underlie solutions to the problem.

Q5 What is your view about the UK regulations on research involving animals in the UK?

The current UK regulations are undoubtedly stringent and serve their purpose by providing strict regulation of the use of animals in research. However, the Royal Society is dissatisfied by the inefficiencies and slowness in granting licences and in administering the law. The validity of scientific project proposals should be judged by fully competent and independent scientific referees who will usually be appointed by funding bodies. However, at present, scientific validity may be assessed in turn by grant-giving bodies, Local Ethical Review Panels and the Home Office. This process imposes unnecessary duplication of effort and results in long delays. The Ethical Review Panels play an important role in taking a broader view of a proposed project but should not be responsible for the assessment of scientific validity. Nor should that be the job of the Home Office, and, wherever possible, information should be obtained from the funding bodies' assessments. If these are not available, a licence could be issued conditional on receiving

satisfactory reports from expert referees. This would then make the process more co-ordinated between the various parties, and help to avoid unnecessary bureaucracy and consequential delays.

The trend towards greater bureaucracy makes carrying out animal experiments more difficult, and may drive research and testing of animals into foreign laboratories with much lower standards than in the UK. The Home Office can help UK scientists by making UK procedures for obtaining licences as fast and efficient as possible, whilst maintaining the current high levels of control. This also relates to the multinational character of research as the Home Office should improve procedures so that experienced scientists from abroad can readily obtain licences when visiting the UK for purposes of scientific collaboration. This would then help promote in other countries the high standards of regulation found in the UK, and encourage sharing of information and technical development.

Q6 What do you think about the information that is available to the public about research involving animals?

The Royal Society stated publicly its views on the use of animals in research in its position statement in 2002 (see Annex 1) and this, and the Society's comments on related issues are published on its web-site. The Society believes that it has a responsibility to publicise the multiple benefits of using animals in research and has done this through giving evidence to the House of Lords Animals in Scientific Procedures Committee, and through the activities of the Royal Society Animals in Research Committee, which is currently preparing a guide for scientists on many of the issues discussed here, which will be published early in 2004. The Royal Society feels that it is important to recognise the need for information to be provided to the public about the benefits to be obtained from the use of animals in research, and for discussions to take place about the use of alternatives and their limitations, and encourages other members of the scientific community to add their voice in support of this work.

Yours sincerely

Sir Patrick Bateson FRS