

The response reproduced below was submitted to the consultation held by the Nuffield Council on Bioethics on the ethics of research involving animals during October-December 2003. The views expressed are solely those of the respondent(s) and not those of the Council.

The Biosciences Federation

INTRODUCTION

The Biosciences Federation (BSF) was founded in December 2002 in order to create a single authority within the life sciences that decision-makers can consult for opinion and information. It brings together the strengths of the Institute of Biology and societies that were formerly members of the UK Life Sciences Committee. The societies that have already joined the BSF (see www.bsf.ac.uk) represent some 60,000 members and cover the whole of life sciences, from physiology, neuroscience, biochemistry and microbiology to ecology.

The Animal Science Group (ASG) of the Biosciences Federation arose out of a series of meetings of interested persons in 1998, initially between representatives of the British Pharmacological Society and the Laboratory Animal Science Association, but later including other groups. The new group was formally adopted as a sub-group of the UK Life Sciences Committee (UKLSC) in November 1998, and the first formal meeting of the group was on 8 January 1999. The present name for the group was adopted at a later 1999 meeting. When the UKLSC was subsumed by the Biosciences Federation in late 2002, the Animal Science Group was transferred to the new body.

The present response was prepared by the Animal Science Group with the approval of the Biosciences Federation. The BSF view on the use of living animals in education and research is outlined in Appendix A

QUESTION 1 – What is your view of the use of animals in research?

Research involving animals provides vital information that cannot currently be obtained by any other method, and has helped in the development of many life-saving medical and veterinary treatments. It is a requirement under UK law that animal experiments are *only* undertaken when there is no viable alternative. Consequently, the BSF agrees with the conclusions in the 2002 report from the House of Lords Select Committee on Animals in Scientific Procedures that “there is a continued need for animal experimentation both in applied research and in research aimed purely at extending knowledge”, and that “toxicological testing in animals is at present essential for medical practice and the protection of consumers and the environment”.

There are numerous examples of research on animals that have increased our knowledge and understanding of biological processes, and which have been acclaimed as leading to major breakthroughs in medicine and surgery for animals and humans (see Appendix B for a few examples). These demonstrate that research on animals can often be transferred to humans, but does not necessarily mean that *all* research on animals can *always* be transferred to humans. This research might nevertheless help us to understand the key differences between animals and humans. By increasing our understanding of the behaviour and diseases of animals it also contributes to the development of new veterinary treatments, and may also be necessary for the conservation of endangered species.

Yes, the acceptability of using animals does depend on the purpose of the research. Research aimed at addressing trivial questions (whether in basic biology or in clinically relevant areas) is difficult to justify. Research in areas of high disease burden (clinical or veterinary) or of great socioeconomic impact (e.g. potential environmental toxins) may be considered of higher priority. However, major developments in medicine and surgery have often been based on fundamental understanding of biological premises. These have required “blue skies” research, which, by definition, has no immediate or obvious application.

Different types of research often require the use of different animals. As examples, our understanding of genetics, developmental biology and structural biology owes much to research on lower species including flies and worms. In contrast, major developments in complex diseases of the nervous system, development of vaccines or new treatments has relied on more advanced species, including primates.

The extent to which animals suffer during research varies considerably depending on the animal, the nature of the research and the definition of suffering. Some would argue that even housing animals in family groups in an enriched environment, and meeting all their needs, constitutes "suffering" in the sense that they are not living in their natural habitat, or that humane killing of healthy animals confers suffering. Most scientists would not fully share this view. Nevertheless scientists must be aware of the full spectrum of potential suffering including the effects of keeping animals in captivity. This, in itself, is an important area for research.

It is difficult to define unacceptable levels of suffering outside the issue of need/benefit, but it is important to point out that all experimental animals used in the UK are housed in humane conditions, are well looked after, and the vast majority are killed humanely with no other suffering. The nature of some research (e.g. to minimise disease or in toxicity studies) by necessity causes pain and discomfort. However, under current UK law such studies require special justification, stringent limits on numbers and species, close monitoring and veterinary involvement, and defined humane end points.

It seems to us that similar cost/benefit analysis should apply to *all* aspects of the interaction of humans and animals within our society. Approximately 2.75 million animals are used each year in experiments, 85% of which are rodents. However, there were 935 million registered slaughterhouse deaths of poultry in the UK in 2002, plus at least 80 million day old chick deaths. Therefore, this use of chicken outnumbers experimental animal deaths by some 250:1. Many other animal species are also killed for food, as pests, accidentally as a result of human activities, by pet animals, or for sport. A striking example of one of the latter categories, are figures reported by the British Mammals Society that over 300 million animals are killed by domestic cats each year (a total which they suggest is an underestimate!).

It is important to recognise that the UK has the strictest legislation on animal experimentation, and this is rigorously enforced. The scientific community accepts the aims of the legislation but opposes further restrictions unless major benefits to animal welfare can be demonstrated. It should also be noted that some of the bureaucracy associated with the legislation may actually impede medical research, and yet have no obvious relevance to animal welfare.

Thus we should be encouraging the use of animal experiments in the UK where standards of welfare are high, rather than take actions which might lead to research moving to countries with much lower standards of animal care.

QUESTION 2 – what are your views about the use of genetically modified animals in research?

GM animals have already proven enormously valuable in biomedical research. In many cases they have allowed a reduction in the number of animals exposed to experimental intervention, and the vast majority of GM animals have no obvious phenotypic features and no adverse responses. Nevertheless GM animals do raise new and different issues because of the unpredictability of some manipulations on phenotypes, and because in some cases significant numbers are required for breeding.

GM animals might be considered 'unnatural' in the sense that they are created by human intervention. But this is not too different from farm animals, pets and other animals that are

selectively bred for specific phenotypes. The same concerns apply to each of these latter interventions; i.e. the production of animals with phenotypes which cause harm or suffering, and the possible impact of their integration with those in the wild.

One example of animals which were created to develop chronic diseases would include GM mice that mimic Alzheimer's Disease. Another would be mice with modifications in the prion gene, which helped to establish the pathogenesis of prion diseases (CJD and BSE) and the nature of the species barrier. The development of these latter GM mice has largely led to the replacement of the need to use primates, sheep, goats, and cows in this area of research.

The guidance on assessing the welfare of GM animals has been reviewed recently, and ongoing discussions and recent reviews of practises, are attempting to improve the detection of subtle changes in phenotypes which may impact on animal welfare. See "The use of genetically modified animals" (The Royal Society, 2001); "Report on animals and biotechnology" (Agriculture and Environment Biotechnology Commission, 2002); "Report on biotechnology" (Animal Procedures Committee, 2001); "Genetically modified and cloned animals: all in a good cause?" (Genewatch, 2002).

QUESTION 3 - What is your view about use of alternatives?

There is extensive research into alternatives that is ongoing within all areas of research, but because it is often embedded within research programmes (whether these use animals or not) it is not defined as "research into alternatives". An excellent example of this would be the major advances in sophisticated imaging techniques (e.g. MRI, PET). The MRI technique, the development of which merited the recent award of Nobel prizes, has provided an important alternative method to the use of experimental animals in some research areas.

Industry has expended great effort and money in developing alternatives, particularly in toxicity testing. It is notable that while the volume of biomedical research in the UK has increased dramatically over the last two decades, the number of research animals used has almost halved.

In general, the funding and conduct of research into alternatives is best achieved within high quality research programmes rather than under a separate category.

Some duplication of animal research is essential. Without replication of scientific findings there can be limited confidence in the results. However, there is a problem with repetition of experiments which yield negative data or which fail to replicate a published finding, because it is difficult to get such work accepted for publication in peer reviewed journals. Sharing of data is to be encouraged, but without quality assessment (e.g. by peer review), it may have limited utility.

Publication of research involving animals in scientific journals could be improved by including better discussion of the techniques used, of the difficulties encountered, of humane endpoints, of adverse effects, and of statistical planning and justification. This is largely in the hands of editors who often have space limitations in the publications they edit.

QUESTION 4 - What is your view about ethical issues relating to the use of animal in research?

In general, we maintain that the current arrangements for the ethical approval of research projects on animals in the UK are exemplary. Each project carried out under the Animals (Scientific Procedures) Act, 1986 must be approved by an Ethical Review Group representing the establishment in which the research is to be carried out. The establishment's Ethical Review Process (ERP) must first be approved by the Home Secretary. Ethical issues are also taken into account by Home Office Inspectors during their consideration of applications for project licences. We naturally would *not* support any

research using animals that was scientifically flawed. There are some areas of research that would probably never be licensed in the UK.

The development and institution of the ERP in 1999 has helped to address ethical issues, as any research project that might cause suffering to animals *must* be given ethical approval by a group independent of those carrying out the research. This Ethical Review Group is expected to include lay members representing the interests and views of the general public. The ethical considerations should include the cost to the animals, in the form of pain and suffering, and the potential gains and benefits to humans and other animals that might come from the research, leading to advances in knowledge, and improvements in medical and veterinary treatments. Ethical approval of a project *must* depend upon the potential benefits outweighing the likely costs. In practice this calculation is often difficult, as it is subjective and imprecise. The outcome may depend, for example, on whether or not the death of an animal is considered a cost even when this involves humane killing. Since the vast majority of animals used in research would not be born were they not needed for this purpose, and would not have lived freely in the wild, there is no alternative positive outcome against which humane death can be costed.

It is worth noting that the Animal Science Group of the Biosciences Federation has developed a document outlining suggestions for best practice for the Ethical Review Process. This was accepted by the Home Office Inspectorate, and is posted on the ASG section of the BSF website (see Appendix C). There are also numerous articles on the ethics of animal use in research (for an example see Appendix D).

QUESTION 5 - What is your view about the UK regulation in research involving animals in the UK?

Current provisions for the assessment of welfare of animals are rigorous and of high quality, but must be continuously revised and improved as our knowledge and understanding increases and new examples of best practice emerge. Assessments of welfare should be conducted before, during and after a project. This should be a continuous activity. Regulations can only provide principles and guidelines for welfare assessments. Assessments must rely on involving experts from different backgrounds, and continued evaluation.

The cost/benefit analysis has been the subject of a recent, quite intensive review by the Animal Procedures Committee. The results of that review suggest that the system is reasonably robust but with scope for possible improvement. We agree with this conclusion and the recognition by the APC that cost/benefit analysis is inevitably imprecise and based ultimately on subjective judgement. One concern is that cost/benefit analysis is generally (with the exception of experiments with adverse effects, which are classed as substantial, or those using primates) based on the judgement of individual inspectors. The experience and expertise of such inspectors varies considerably and there is concern amongst the scientific community that some have limited experience of scientific research (which would include a PhD and postdoctoral research).

Cost/benefit analysis, like animal welfare, should be an ongoing process which is interactive and should take into account unexpected adverse effects and scientific outcomes. This, as with many other aspects of research on animals, should be a continuing dialogue rather than a snapshot assessment.

Results should, in principle, be published, but the vehicle for publication is important. To be effective scientific findings should attract the interest of other researchers in the field. Findings about animal welfare need to reach a different audience.

We are aware of individuals who have already moved abroad or who have transferred their research abroad, and of companies who are relocating their animal studies outside the UK (a few are willing to speak out about this, but many are not willing because of concerns about their UK position). This is a major concern, but one which cannot justifiably be ascribed entirely to UK regulations. Most scientists welcome the rigour of UK legislation on animal research and object only when they see regulations that prove a major burden with no obvious benefits to animals. The exit of animal research, researchers and companies may be in part due to legislation and bureaucracy, but also reflects issues of sensitivity and safety in the UK due to minority pressure groups.

QUESTION 6 - What do you think about the information that is available to be published about research involving animals?

This question is probably directed primarily to non-scientists, but the Federation has strong views.

We believe that the public does not receive sufficient information on animal experiments and legislation. This is supported by recent, extensive MORI polls. For example, many respondents are willing to support animal experiments but only if stringent legislation, regulation and reviews are in place. Such processes are in place, but the public is unaware of them.

There are a limited number of scientists who are willing to speak openly about research involving animals. Scientists already work very long hours and have many demands on their time, and open discussion on animals is difficult, sensitive, and can attract threats to the individual, their staff and families. There is no reward for this activity. Consequently it is necessary to encourage and reward scientists who talk to the public about this sensitive topic.

The Biosciences Federation also submitted to the Council the following materials:

Appendix A

Biosciences Federation statement on the use of living animals in education and research.

Appendix B

Useful information on the importance of animal use in medical and veterinary advances.

Appendix C

The Ethical review process - suggestions on best practice for processing licences.

Appendix D

Stafleu, F.R., Tramper, R., Vorstenbosch, J., and J.A. Joles. (1999). "The ethical acceptability of animal experiments. A proposal for a system to support decision-making". *Laboratory Animals* 33 (March 1999), pp. 295-303.