

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 Wellcome Trust, UK

**December 2003**

### **Introduction**

1. The Wellcome Trust (the "Trust") is an independent biomedical research charity, established under the will of Sir Henry Wellcome. In the financial year ending 30 September 2002, the Trust's expenditure on research grants was more than £400 million, the majority of which was in the UK.
2. Around one quarter of the biomedical research projects supported by the Trust involve the use of animals, with the vast majority of these using rats and mice. The Trust's current position statement on the use of animals in medical research is shown in Appendix A.

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

3. Research using animals has made an important contribution to advances in medicine and surgery, resulting in major improvements in the health of human beings and animals.
4. The Trust will support biomedical and veterinary research using animals in the UK providing:
  - it is fully compliant with current Home Office legislation;
  - it has been approved by a local ethics committee;
  - it has been successfully independently peer reviewed; and
  - due consideration has been given to the refinement, reduction or replacement of the animals in the experiment and no viable non-animal alternatives exist.
5. International research supported by the Trust is expected to be carried out in the spirit of the UK legislation, as well as being compliant with all local legislation and ethical review procedures.
6. Whilst supporting the ongoing development of reduction, refinement or replacement (the 3Rs), the Trust is of the opinion that animal experimentation will continue to play a key role in essential research towards tackling major medical problems. Currently, for certain types of medical research there are no viable alternatives to using animal models.
7. The development of disease frequently involves complex interactions between different systems or organs within the body. In these instances, studies using alternatives to animals (including cell lines, tissue cultures or whole organs, computer modelling and human studies) can only provide limited information and a fuller understanding requires studies at the whole-body level. For some types of fundamental research, such as research on the control of physiological processes or where organ to organ communication plays an important role, there are no alternative approaches to using animals.

8. The Trust would agree that the use of alternatives to animals can often provide useful information in research or toxicity testing, particularly where a whole animal approach might not be essential. However, when researching complex diseases or testing new treatments in the form of drugs or therapies, it is obviously not possible to assess the effect on the whole animal by simply using one cell or tissue type. Again, much of the fundamental research which underpins more applied research depends on observing what happens in whole animals.
9. The Trust considers, therefore, that for the kind of research that provides the most hope for understanding health and disease and the development of new treatments, it is currently difficult to foresee a time when it might be possible to conduct this research without using animals.
10. Some people argue that animals are misleading to use as models of human disease; however, as knowledge about genetics has increased, it has now been shown that humans and animals have a similar genetic makeup. For example, mice share over 85% of the sequences of their genes with humans and there are analogous genes in the mouse for nearly every human gene. This means that many biochemical pathways are identical, or similar, in animals and humans.
11. Of course no animal can provide a perfect model for human disease, which is why all discoveries based on animal research, once they are at a well developed stage, are eventually tested on human volunteers before being used for treating patients. However, animal research allows us to understand the dynamics of health and disease in a whole organism, which increases the chance of developing suitable treatments for human patients.

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

12. Genetically modified (GM) animals provide valuable models of human disease where no naturally occurring models exist, and they help researchers to explain disease pathways and assess potential new therapies. The result of our ability genetically to manipulate animals (mostly mice and rats) to mimic a variety of human diseases is likely to lead to treatments for many of these diseases.
13. The need to deliberately create an animal with a condition which will inevitably cause it discomfort should be justified in the same way as any other proposed research under the terms of the Animals (Scientific Procedures) Act 1986. The level of care of GM animals must always be appropriate to the needs of the animal.
14. The Trust does not consider that GM animals should be necessarily seen as “unnatural”. Mutations arise spontaneously in animals in nature and often, when the phenotypic result of these natural mutations is considered advantageous or appealing by humans, then these mutated animals are selected and bred. Obvious examples are the various breeds of dogs that can be observed at Crufts and the selection of traits in farm animals related to food production. All traits established by breeding have a genetic basis for that trait.
15. The same is true for inbred mouse strains used in research, where natural mutations or even induced mutations (for example by gene targeting or chemical mutagenesis) have been selected. For example, the non-obese diabetic (NOD) inbred mouse strain originated from breeding pairs of mice exhibiting a natural borne tendency to diabetes,

and now the inbred strain can develop diabetes within four weeks of age. Similarly, a chemically induced mutated mouse strain is susceptible to deafness and can lose the ability to hear within four to six weeks. The speed at which the disease develops in both these strains makes them extremely useful tools for studying the disease and developing potential treatments.

16. The main difference between dog breeds, inbred strains and GM animals (the vast majority of which are mice) is that the mutations in the GM animals have been purposefully introduced by humans, as opposed to leaving it to nature, in order to develop a particular trait that makes them more or less susceptible to particular diseases, such as cancer, diabetes, rheumatoid arthritis etc. In fact, with GM animals, usually only one specific gene is targeted for modification, so the effects on physiology and development may be more accurately predicted than animals which result from selective breeding or chemical mutagenesis.

#### **What is your view about the use of alternatives?**

17. The development of alternatives to animals continues on many fronts and their use is increasing, but no methods can satisfactorily replace animals in all cases, as explained in response to the first question. Animal use will need to continue, although the continued development of new techniques, such as cell lines and computer modelling, will reduce the need for animal research in some areas. The approval for the use of human embryos in research may allow the development of new human cell lines which may reduce the need to use animals in some research areas. However, the use of animals will be increasingly important in post-genome research and it is expected that the numbers of animals used in research, particularly mice and rats, will increase substantially due to the increased use of GM animals.
18. Scientists have developed, and will continue to develop, non-animal techniques as a natural corollary to, or by-product of, their research. However, developing and promoting them as alternatives (to specific animal procedures) is not often the main objective of these scientists. Many of the non-animal methods in use in biomedical research were not developed specifically as "alternatives". For example, cell culture was developed originally as a method for studying cell biology and events at the cellular level, not as an 'alternative to using animals' - but certain specific applications, such as monoclonal antibody production, have become alternatives to animal methods.

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

19. At a practical level, all animal researchers have a duty to reduce suffering to a minimum. Good husbandry is as vital to the researcher as his/her experimental protocol. The law recognizes that animals have interests in being treated humanely and in being kept from unnecessary suffering. It must also be noted that research using animals does not always take place solely for human benefit, but can also be of benefit to animals, for example in the development of veterinary medicines. The Trust is a major funder of research for the benefit of animal health.
20. The Trust considers that the existing cost/benefit assessment is reasonable, but that the assessment of scientific validity of proposed experiments should remain primarily the responsibility of the expert scientific community. The main strength of the cost/benefit assessment is that it ensures that a project licence is only granted by the Home Office if

the potential benefits of the proposed research outweigh the costs. This assessment is necessarily subjective but it does allow decisions to be made on a case-by-case basis. It is important to recognise that circumstances can change dramatically, particularly in such a dynamic field as biomedical science, for example through the emergence of new diseases (e.g. BSE in cattle and the emergence of new variant Creutzfeld-Jakob disease, nvCJD, in humans). This can lead to unforeseen justifications for the use of a particular species or procedure, which might not previously have been deemed to be justifiable under the existing cost/benefit assessment.

21. Since its introduction in April 1999, the Trust considers that the Ethical Review Process (ERP) has helped researchers to focus on the broader ethical issues relating to their work with animals. The process necessitates the researchers spending more time justifying their research, including justifying all of the proposed procedures and why alternatives are not suitable. The presence of a lay member on the ethical review committee helps to demonstrate to the public that research using animals in the UK is governed by strict ethical guidelines.
22. The ERP was introduced with the intention that its implementation should not result in a duplication of effort or undue delay on behalf of both the local ethical review committee and the Home Office Inspectorate. However, the main weaknesses of the ERP seem to be the increased time spent by researchers on justifying their research and the increased delays in the processing of new project licence applications and renewals to project licences.

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

23. The UK has some of the most stringent regulations in the world on the use of animals in research, particularly in the field of biomedical research. The Trust considers that UK legislation on animal procedures should not be made more restrictive or complex as this may drive some of the UK's best scientists abroad and deter overseas scientists from working in the UK. This would have serious implications for research capacity in the UK, particularly in the post-genomic era, and would have an adverse effect on the UK economy.
24. The Trust is also concerned that the Home Office treats the production of all GM animals as independent procedures that require both authorisation under a project licence and special welfare considerations. It should be noted that the inclusion of "normal" animals used as part of the breeding programme substantially increases the total numbers of animals used as defined by the Home Office statistics. This might give misleading indications that the use of animals in research is increasing more substantially than is really so.
25. The Trust considers that, even with the likely increased use of GM animals in biomedical research over the next decade or so, existing regulatory controls are satisfactory in terms of protecting the welfare of such animals. The Trust would be concerned if further regulations were imposed on research on animals generally, but particularly research that used transgenic technology.
26. The Trust is also aware that UK scientists are concerned about the stringent regulations associated with movement and importation of well-characterised transgenic animals. Whilst they agree that, in some cases, there is a need for transgenic animals to have a

'superior' health status or to be afforded a higher level of care, there is no reason why phenotypically 'normal' transgenic animals should be subject to the same stringent level of import/transport regulations. Reducing the barriers to the international movement of such animals could help to reduce both duplication of research programmes and the numbers of animals used in research.

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

27. Public attitude studies, conducted by MORI in 1999, 2000 and 2002, show that the majority of people in the UK are Conditional Acceptors of the use of animals for medical research, i.e. they accept it if key conditions are fulfilled. The studies show that the proportion of people defined as Conditional Acceptors increased from 82% in 2000 to 90% in 2002<sup>1</sup>. In 2002, MORI, on behalf of the Wellcome Trust, conducted a research study on 11-16 year olds which found that 61% were Conditional Acceptors<sup>2</sup>. The results are lower for this age group due to the higher proportion of children having no comment. The key points on which conditional acceptance is based include the minimisation or elimination of animal suffering and the use of alternatives wherever possible. The Trust considers that there is a lack of knowledge among the general public about how the current legislation operates, and that more information needs to be made available which demonstrates to the public how these key conditions are already being met.
28. The Trust considers that a continued dialogue on the use of animals in research is healthy and should be supported, and that the research community should explain the methods and aims of its research. The MORI public attitude studies in 1999, 2000 and 2002 indicate that public trust of scientists with regard to animal experiments increased substantially between 1999 and 2002, and that there is a link between levels of public trust and perceptions of openness from the scientific community. The Trust therefore considers that those involved in biomedical research using animals need to be as open and transparent as possible, while at the same time being aware of the need to protect researchers from intimidation from extremist groups.

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<sup>1</sup> Figures quoted are from the Research Defence Society 2003 Annual Report

<sup>2</sup> Schools Omnibus 2001-2002 (Wave 8). Children's Attitudes towards the Use of Animals in Medical Research: A Research Study among 11-16 Year Olds on behalf of The Wellcome Trust.

[The Wellcome Trust also submitted to the Council their policy on the use of animals in medical and veterinary research and several case studies on the use of animals in medical and veterinary research funded by the Trust]