

The ethics of animal research

Talking Point on the use of animals in scientific research

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Animal research has had a vital role in many scientific and medical advances of the past century and continues to aid our understanding of various diseases. Throughout the world, people enjoy a better quality of life because of these advances, and the subsequent development of new medicines and treatments—all made possible by animal research. However, the use of animals in scientific and medical research has been a subject of heated debate for many years in the UK. Opponents to any kind of animal research—including both animal-rights extremists and anti-vivisectionist groups—believe that animal experimentation is cruel and unnecessary, regardless of its purpose or benefit. There is no middle ground for these groups; they want the immediate and total abolition of all animal research. If they succeed, it would have enormous and severe consequences for scientific research.

No responsible scientist wants to use animals or cause them unnecessary suffering if it can be avoided, and therefore scientists accept controls on the use of animals in research. More generally, the bio-science community accepts that animals should be used for research only within an ethical framework.

The UK has gone further than any other country to write such an ethical framework into law by implementing the Animals (Scientific Procedures) Act 1986. It exceeds the requirements in the European Union's Directive 86/609/EEC on the protection of animals used for experimental and other scientific purposes, which is now undergoing revision (Matthiessen *et al.*, 2003). The Act requires that proposals for research involving the use of animals must be fully

assessed in terms of any harm to the animals. This involves detailed examination of the particular procedures and experiments, and the numbers and types of animal used. These are then weighed against the potential benefits of the project. This cost-benefit analysis is almost unique to UK animal research legislation; only German law has a similar requirement.

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In addition, the UK government introduced in 1998 further 'local' controls—that is, an Ethical Review Process at research institutions—which promote good animal welfare and humane science by ensuring that the use of animals at the designated establishment is justified. The aims of this additional review process are: to provide independent ethical advice, particularly with respect to applications for project licences, and standards of animal care and welfare; to provide support to licensees regarding animal welfare and ethical issues; and to promote ethical analysis to increase awareness of animal welfare issues and to develop initiatives for the widest possible application of the 3Rs—replacement, reduction and refinement of the use of animals in research (Russell & Burch, 1959). In practice, there has been concern that the Ethical Review Process adds a level of bureaucracy that is not in proportion to its contribution to improving animal welfare or furthering the 3Rs.

Thanks to some extensive opinion polls by MORI (1999a, 2002, 2005), and subsequent polls by YouGov (2006) and ICM (2006), we now have a good understanding of the public's attitudes towards animal research. Although society views animal research as an ethical dilemma, polls show that a high proportion—84% in 1999, 90% in 2002 and 89% in 2005—is ready to accept the use of animals in medical research if the research is for serious medical purposes, suffering is minimized and/or alternatives are fully considered. When asked which factors should be taken into account in the regulatory system, people chose those that—unknown to them—are already part of the UK legislation. In general, they feel that animal welfare should be weighed against health benefits, that cosmetic-testing should not be allowed, that there should be supervision to ensure high standards of welfare, that animals should be used only if there is no alternative, and that spot-checks should be carried out. It is clear that the UK public would widely support the existing regulatory system if they knew more about it.

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Unsurprisingly, medical general practitioners (GPs) are even more aware of the contribution that animal research has made and continues to make to human health. In 2006, a survey by GP Net showed that 96% of GPs agreed that animal research



has made important contributions to many medical advances (RDS News, 2006). The opinion poll also sought doctors' views about the safety testing of medicines. Almost nine out of ten GPs (88%) agreed that new medicines should be tested on animals before undergoing human trials.

GP Net also asked whether GPs agreed that "medical research data can be misleading"; 93% agreed. This result puts into context the results from another poll of GPs in 2004. Europeans for Medical Progress (EMP; London, UK), an anti-vivisection group, found that 82% had a "concern [...] that animal data can be misleading when applied to humans" (EMP, 2004). In fact, it seems that most GPs think that medical research in general can be misleading; it is good scientific practice to maintain a healthy degree of scepticism and avoid over-reliance on any one set of data or research method.

Another law, which enables people to get more information, might also help to influence public attitudes towards animal research. The UK Freedom of Information (FOI) Act came into full force on 1 January 2005. Under the Act, anybody can request information from a public body in England, Wales or Northern Ireland. Public bodies include government departments, universities and some funding bodies

such as the research councils. The FOI Act is intended to promote openness and accountability, and to facilitate better public understanding of how public authorities carry out their duties, why and how they make decisions, and how they spend public money. There are two ways in which information can be made available to the public: some information will be automatically published and some will be released in response to individual requests. The FOI Act is retrospective so it applies to all information, regardless of when it was created.

In response to the FOI Act, the Home Office now publishes overviews of all new animal research projects, in the form of anonymous project licence summaries, on a dedicated website. This means that the UK now provides more public information about animal research than any other country. The Research Defence Society (RDS; London, UK), an organization representing doctors and scientists in the debate on the use of animals in research and testing, welcomes the greater openness that the FOI Act brings to discussions about animal research. With more and reliable information about how and why animals are used, people should be in a better position to debate the issues. However, there are concerns that extremist groups will try to obtain personal details and information that can identify researchers, and use it to target individuals.

As a House of Lords Select Committee report in July 2002 stated, "The availability to the public of regularly updated, good quality information on what animal experiments are done and why, is vital to create an atmosphere in which the issue of animal experimentation can be discussed productively" (House of Lords, 2002). Indeed, according to a report on public attitudes to the biological sciences and their oversight, "Having information and perceived honesty and openness are the two key considerations for the public in order for them to have trust in a system of controls and regulations about biological developments" (MORI, 1999b).

In the past five years, there have been four major UK independent inquiries into the use of animals in biomedical research: a Select Committee in the House of Lords (2002); the Animal Procedures Committee (2003); the Nuffield Council on Bioethics (2005); and the Weatherall Committee (Weatherall *et al*, 2006), which specifically examined the use of non-human primates in scientific and medical research. All committees included non-scientists and examined evidence from both sides of the debate. These rigorous independent inquiries all accepted the rationale for the use of animals in research for the benefit of human health, and concluded that animal research can be scientifically validated on a case-by-case basis. The Nuffield Council backed the 3Rs and the need for clear information to support a constructive debate, and further stated that violence and intimidation against researchers or their allies is morally wrong.

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In addition, the Advertising Standards Authority (ASA; London, UK) has investigated and ruled on 38 complaints made since 1992 about published literature—leaflets and brochures—regarding claims about the validity or otherwise of animal research and the scope of alternative methods. In 34 out of 38 cases, they found against the anti-vivisectionist groups, either supporting complaints about anti-vivisectionist literature, or rejecting the complaints by anti-vivisectionists about the

literature from medical organizations. Only four complaints against scientific/medical research literature have been upheld, not because the science was flawed but as a result of either semantics or the ASA judging that the advertisement fell outside the UK remit.

Animal-rights groups also disagree with the 3Rs, since these principles still allow for the use of animals in research; they are only interested in replacement

However, seemingly respectable mainstream groups still peddle dangerously misleading and inaccurate information about the use of animals in research. As previously mentioned, EMP commissioned a survey of GPs that showed that the “majority of GPs now question the scientific worth of animal tests” (EMP, 2004). The raw data is available on the website of EMP’s sister group Americans For Medical Advancement (AFMA; Los Angeles, CA, USA; AFMA, 2004), but their analysis is so far-fetched that the polling company, TNS Healthcare (London, UK), distanced itself from the conclusions. In a statement to the Coalition for Medical Progress (London, UK)—a group of organizations that support animal research—TNS Healthcare wrote, “The conclusions drawn from this research by AFMA are wholly unsupported by TNS and any research findings or comment published by AFMA is not TNS approved. TNS did not provide any interpretation of the data to the client. TNS did not give permission to the client to publish our data. The data does not support the interpretation made by the client (which in our opinion exaggerates anything that may be found from the data)” (TNS Healthcare, 2004). Nonetheless, EMP has used its analysis to lobby government ministers and misinform the public.

Approximately 2.7 million regulated animal procedures were conducted in 2003 in the UK—half the number performed 30 years ago. The tight controls governing animal experimentation and the widespread implementation of the 3Rs by the scientific community is largely responsible for this downward trend, as recognized recently by then Home Office Minister, Caroline Flint: “...new technologies in developing drugs [have led] to sustained

and incremental decreases in some types of animal use over recent years, whilst novel medicines have continued to be produced. This is an achievement of which the scientific community can be rightly proud” (Flint, 2005).

After a period of significant reduction, the number of regulated animal procedures stabilized from 1995 until 2002. Between 2002 and 2005, the use of genetically modified animals—predominantly mice—led to a 1–2% annual increase in the number of animals used (Home Office, 2005). However, between 1995 and 2005, the growth in UK biomedical research far outstripped this incremental increase: combined industry and government research and development (R&D) spending rose by 73% from £2,080 million to £3,605 million (ABPI, 2007; DTI, 2005). Animal research has obviously become a smaller proportion of overall bioscience and medical R&D spending in the UK. This shows the commitment of the scientific community to the development and use of replacement and reduction techniques, such as computer modelling and human cell lines. Nevertheless, animal research remains a small, but vital, part of biomedical research—experts estimate it at about 10% of total biomedical R&D spending.

The principles of replacing, reducing and refining the use of animals in scientific research are central to UK regulation. In fact, the government established the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs; London, UK) in May 2004 to promote and develop high-quality research that takes the 3Rs into account. In support of this, then Science Minister Lord Sainsbury announced in 2005 that the Centre would receive an additional £1.5 million in funding over the next three years.

The ultimate aim of the NC3Rs is to substitute a significant proportion of animal research by investigating the development of alternative techniques, such as human studies, and *in vitro* and *in silico* studies. RDS supports this aim, but believes that it is unrealistic to expect this to be possible in every area of scientific research in the immediate future. After all, if the technology to develop these alternatives is not available or does not yet exist, progress is likely to be slow. The main obstacle is still the difficulty of accurately mimicking the

complex physiological systems of whole living organisms—a challenge that will be hard to meet. There has been some progress recently imitating single organs such as the liver, but these need further refinement to make them suitable models for an entire organ and, even if validated, they cannot represent a whole-body system. New and promising techniques such as microdosing also have the potential to reduce the number of animals used in research, but again cannot replace them entirely.

Anti-vivisectionist groups do not accept this reality and are campaigning vigorously for the adoption of other methods without reference to validation or acceptance of their limitations, or the consequences for human health. Animal-rights groups also disagree with the 3Rs, since these principles still allow for the use of animals in research; they are only interested in replacement. Such an approach would ignore the recommendations of the House of Lords Select Committee report, and would not deal with public concerns about animal welfare. Notwithstanding this, the development of alternatives—which invariably come from the scientific community, rather than anti-vivisection groups—will necessitate the continued use of animals during the research, development and validation stages.

Society should push authorities to quickly adopt successfully validated techniques, while realizing that pushing for adoption without full validation could endanger human health

The scientific community, with particular commitment shown by the pharmaceutical industry, has responded by investing a large amount of money and effort in developing the science and technology to replace animals wherever possible. However, the development of direct replacement technologies for animals is a slow and difficult process. Even in regulatory toxicology, which might seem to be a relatively straightforward task, about 20 different tests are required to assess the risk of any new substance. In addition, introducing a non-animal replacement technique involves not only development of the method, but also its validation by national and international regulatory authorities.

These authorities tend to be conservative and can take many years to write a new technique into their guidelines. Even then, some countries might insist that animal tests are carried out if they have not been explicitly written out of the guidelines. Society should push authorities to quickly adopt successfully validated techniques, while realizing that pushing for adoption without full validation could endanger human health.

Despite the inherent limitations of some non-animal tests, they are still useful for pre-screening compounds before the animal-testing stage, which would therefore reduce rather than replace the number of animals used. An example of this is the Ames test, which uses strains of the bacterium *Salmonella typhimurium* to determine whether chemicals cause mutations in cellular DNA. This and other tests are already widely used as pre-screens to partly replace rodent testing for cancer-causing compounds. Unfortunately, the *in vitro* tests can produce false results, and tend to be used more to understand the processes of mutagenicity and carcinogenicity than to replace animal assays. However, there are moves to replace the standard mouse carcinogenicity assay with other animal-based tests that cause less suffering because they use fewer animals and do not take as long. This has already been achieved in tests for acute oral toxicity, where the LD50—the median lethal dose of a substance—has largely been replaced by the Fixed Dose Procedure, which was developed, validated and promoted between 1984 and 1989 by a worldwide collaboration, headed by scientists at the British Toxicological Society (Macclesfield, UK).

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Furthermore, cell-culture based tests have considerably reduced the use of rodents in the initial screening of potential new medicines, while speeding up the process so that 10–20 times the number of compounds can be screened in the same period. A leading cancer charity, Yorkshire Cancer

Research (Harrogate, UK), funded research into the use of cell cultures to understand better the cellular mechanisms of prostate cancer—allowing researchers to investigate potential therapies using fewer animals.

Microdosing is an exciting new technique for measuring how very small doses of a compound move around the body. In principle, it should be possible to use this method in humans and therefore to reduce the number of animals needed to study new compounds; however, it too has limitations. By its very nature, it cannot predict toxicity or side effects that occur at higher therapeutic doses. It is an unrealistic hope—and a false claim—that microdosing can completely replace the use of animals in scientific research; “animal studies will still be required,” confirmed the Fund for the Replacement of Animals in Medical Experiments (FRAME; Nottingham, UK; FRAME, 2005).

However, as with many other advances in non-animal research, this was never classified as ‘alternatives research’. In general, there is no separate field in biomedical research known as ‘alternatives research’; it is one of the highly desirable outcomes of good scientific research. The claim by anti-vivisection campaigners that research into replacements is neglected merely reflects their ignorance.

Good science and good experimental design also help to reduce the number of animals used in research as they allow scientists to gather data using the minimum number of animals required. However, good science also means that a sufficient number must be used to enable precise statistical analysis and to generate significant results to prevent the repetition of experiments and the consequent need to use more animals. In 1998, FRAME formed a Reduction Committee, in part to publicize effective reduction techniques. The data collected by the Committee so far provides information about the overall reduction in animal usage that has been brought about by the efforts of researchers worldwide (FRAME Reduction Committee, 2005).

For example, screening potential anti-cancer drugs uses the so-called hollow-fibre system, in which tumour cells are grown in a tube-like polymer matrix that is implanted into mice. Drugs are then administered, the tubes removed and the number of cells determined. This system has increased the amount of data that can be obtained per

animal in some studies and has therefore reduced the number of mice used (Double, 2004). In neuroscience, techniques such as cooling regions of the brain instead of removing subsections, and magnetic resonance imaging, have both helped to reduce the number of laboratory animals used (Royal Society, 2004).

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Matching the number of animals generated from breeding programmes to the number of animals required for research has also helped to reduce the number of surplus animals. For example, the cryopreservation of sperm and oocytes has reduced the number of genetically modified mice required for breeding programmes (Robinson *et al*, 2003); mice lines do not have to be continuously bred if they can be regenerated from frozen cells when required.

Although animals cannot yet be completely replaced, it is important that researchers maximize reduction and refinement. Sometimes this is achieved relatively easily by improving animal husbandry and housing, for example, by enriching their environment. These simple measures within the laboratory aim to satisfy the physiological and behavioural needs of the animals and therefore maintain their well-being.

Another important factor is refining the experimental procedures themselves, and refining the management of pain. An assessment of the method of administration, the effects of the substance on the animal, and the amount of handling and restraint required should all be considered. Furthermore, careful handling of the animals, and administration of appropriate anaesthetics and analgesics during the experiment, can help to reduce any pain experienced by the animals. This culture of care is achieved not only through strict regulations but also by ensuring that animal technicians and other workers understand and adopt such regulations. Therefore, adequate training is an important aspect of the refinement of animal research, and should continually be reviewed and improved.

In conclusion, RDS considers that the use of animals in research can be ethically and morally justified. The benefits of animal research have been enormous and it would have severe consequences for public health and medical research if it were abandoned. Nevertheless, the use of the 3Rs is crucial to continuously reduce the number and suffering of animals in research. Furthermore, a good regulatory regime—as found in the UK—can help to reduce further the number of animals used. Therefore, we support a healthy and continued debate on the use of animals in research. We recognize that those who oppose animal experimentation should be free to voice their opinions democratically, and we look forward to constructive discussion in the future with organizations that share the middle ground with us.

REFERENCES

ABPI (2007) *Facts & Statistics from the Pharmaceutical Industry*. London, UK: Association of the British Pharmaceutical Industry. <http://www.abpi.org.uk/statistics/section.asp?sect=3>

AFMA (2004) *New Survey Among Doctors Suggests Shift in Attitude Regarding Scientific Worth of Animal Testing*. Listed as EFMA Survey of 500 General Practitioners. Los Angeles, CA, USA: Americans For Medical Advancement. www.curedisease.com

Animal Procedures Committee (2003) *Review of Cost-Benefit Assessment in the Use of Animals in Research*. London, UK: Animal Procedures Committee. www.apc.gov.uk

Double JA (2004) A pharmacological approach for the selection of potential anticancer agents. *Altern Lab Anim* **32**: 41–48

DTI (2005) *Science Funding SET Statistics*. London, UK: Department of Trade and Industry. www.dti.gov.uk

EMP (2004) *Doctors Fear Animal Experiments Endanger Patients*. Press release. London, UK: Europeans for Medical Progress. www.curedisease.net

Flint C (2005) *Report by the Animal Procedures Committee—Review of Cost Benefit Assessment in the Use of Animals in Research: Ministerial Response*. London, UK: Home Office

FRAME (2005) Human microdosing reduces the number of animals required for pre-clinical pharmaceutical research. *Altern Lab Anim* **33**: 439

FRAME Reduction Committee (2005) *Bibliography of Training Materials on Experimental Design and Statistical Analysis*. Nottingham, UK: Fund for the Replacement of Animals in Medical Experiments. www.frame.org.uk/reductioncommittee/bibliointro.htm

Home Office (2005) *Statistics of Scientific Procedures on Living Animals, Great Britain 2004*. London, UK: Home Office

House of Lords (2002) *Select Committee on Animals in Scientific Procedures, Volume I—Report*. London, UK: The Stationery Office

ICM (2006) *Vivisection survey, conducted on behalf of BBC Newsnight*. London, UK: ICM Research. www.icmresearch.co.uk

Matthiessen L, Lucaroni B, Sachez E (2003) Towards responsible animal research. *EMBO Rep* **4**: 104–107

MORI (1999a) *Animals in Medicine and Science. Research Study Conducted for the Medical Research Council*. London, UK: MORI. www.ipsos-mori.com

MORI (1999b) *The Public Consultation on Developments in the Biosciences. Executive Summary*. London, UK: MORI. www.ipsos-mori.com

MORI (2002) *The Use of Animals in Medical Research. Research Study Conducted for the Coalition for Medical Progress*. London, UK: MORI. www.ipsos-mori.com

MORI (2005) *Use of Animals in Medical Research. Research Study Conducted for Coalition for Medical Progress*. London, UK: MORI. www.ipsos-mori.com

Nuffield Council on Bioethics (2005) *The Ethics of Research Involving Animals*. London, UK: Nuffield Council on Bioethics

RDS News (2006) *GPs Back Animal Research*. London, UK: Research Defence Society

Robinson V et al (2003) Refinement and reduction in production of genetically modified mice: Sixth report of BVA/AFW/FRAME/RSPCA/UFMW Joint Working Group on Refinement. *Lab Anim* **37**: 1–51

Royal Society (2004) *The Use of Non-Human Animals in Research: A Guide for Scientists*. London, UK: The Royal Society

Russell WMS, Burch RL (1959) *The Principles of Humane Experimental Technique*. London, UK: Methuen

TNS Healthcare (2004) *Statement to the Director of Coalition for Medical Progress*. London, UK: TNS Healthcare

Weatherall D, Goodfellow P, Harris J, Hinde R, Johnson L, Morris R, Ross N, Skehel J, Tickell C (2006) *The Use of Non-Human Primates in Research*. London, UK: The Royal Society

YouGov (2006) *Animal Testing*. Daily Telegraph Survey Results. London, UK: YouGov. www.yougov.com



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For more discussion on this topic, see also Gannon F (2007) *Animal rights, human wrongs?* This issue p519.
Rollin BE (2007) *Animal research: a moral science*. This issue p521.