

Promoting consideration of the ethical aspects of animal use and implementation of the 3Rs

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Abstract

This paper summarises the range of opportunities available for critically considering the ethical, animal welfare and 3Rs issues relating to the use of animals in research and testing. It reviews the role of legislators, regulatory bodies, research funding bodies, industry and others in ensuring that the scientific validity, necessity and justification for animal use is rigorously evaluated and that the 3Rs are always fully implemented.

Keywords: ethics, welfare, 3Rs, review, training

Introduction

Research on animals should only take place within a framework that allows for continuous and challenging consideration of the ethical and welfare issues relating to this use of animals. Consideration of whether, and how, animals are used in experiments involves value judgements that may change with time and with the perspectives, priorities, interests and expertise of those making them (and with the context in which they are made). The process is not a 'one-off' event, just involving, for example, a prospective weighing of the harms and benefits of an individual research project. In fact, there are many diverse opportunities at a local, national and international level to ensure the ethical and welfare aspects of using animals in experiments are always carefully considered and that the 3Rs are fully implemented. Each opportunity can add value since it may examine a different aspect of animal use or bring a different perspective to the issues under discussion. Furthermore, focus may be on a specific area of animal use or may consider the use of animals in experiments more generally.

Drawing on experiences primarily from the UK and Europe, this paper provides a brief summary of some of these opportunities, together with suggestions as to what can be achieved in each case.

❖ Legislation

Legislation controlling the use of animals in scientific procedures likely to cause pain, suffering or distress has a vital role to play in providing

a framework for considering whether, and how, animals are used in experiments. The national governments of most developed countries around the world have responded to public concern on this issue by establishing some form of legislation regulating animal use, though the scope and detail of such legislation is highly variable across countries. There are many overarching ethical, scientific and practical animal welfare issues that legislators need to consider when either drawing up new legislation or revising that which already exists. For example, decisions need to be made regarding the *purposes* for which animal use may be considered justified, the *species* and *the stage of development* (e.g. embryos and fetuses) to be covered, as well as the levels of 'acceptable' animal *suffering*¹. A number of countries have established national advisory bodies (e.g. the UK Animal Procedures Committee, the European Group on Ethics in Science and New Technologies) to discuss and advise their legislators on these types of issues. It is vital for such bodies to have a broad membership that ensures a wide range of perspectives is represented - including people whose expertise and priority is animal welfare and ethics.

Legislative frameworks should also provide opportunities for considering the harms and benefits, implementation of the 3Rs and improvement of animal welfare on an individual *project by project* basis. The importance given to, and provisions made for, this currently varies from country to country (see FELASA 2005). In many instances, the place for considering many of these more focused questions

is a national licensing authority. However, a 'local' animal care or ethics committee (encompassed in the UK by the 'ethical review process') aligned with individual research establishments or, for example, 'regional' animal use oversight committees, can also play essential roles in assuring that local - including non legislative - issues and views are dealt with appropriately. As with the national advisory bodies above, it is important for these committees to have a range of perspectives represented and appropriate input from animal welfare specialists and lay persons.

❖ Research funders

A number of different types of organisation provide funding for scientific research which may involve the use of animals. This includes government-funded organisations (e.g. the UK's Medical Research Council) and the charity sector (e.g. The British Heart Foundation, Cancer Research UK, The Wellcome Trust). Grants may be awarded for a single project carried out by an individual scientist or research group, or for research undertaken by a consortium spread across a number of countries (e.g. the European Commission Research Framework Programme).

Much of this funding comes from the public through taxes or donations. Since the use of animals in research is an issue of considerable public concern, it is essential for all funding bodies to be transparent with respect to the research they fund - including publishing information about the potential harms to animals as well as its perceived benefits. The peer review systems established by each body to consider applications for funding should recognise and consider ethical and welfare concerns, as well as the scientific quality of proposals - particularly since good science and good welfare are so intimately linked. Research funders are in an ideal position to improve standards by insisting that applicants identify and give full consideration to ethical issues and implementation of the 3Rs.

Each funding body should also have a clear policy relating to animal use that provides a framework for the research they will and will not consider for funding. The UK Medical Research Council for example, stated that it will not fund research using great apes (MRC 2006) and has set minimum standards for the husbandry and care of other non-human primates in all the research it funds (MRC 2004). Funding bodies need to be prepared to fund measures which will reduce any animal suffering, and make it clear to grant applicants that money can be factored into the grant proposal for implementing these e.g. through improving animal housing, providing environmental enrichment, or animal or staff training.

In all of the activities detailed above (e.g.

establishing a funding policy, system of peer review etc.) it is important for funding bodies to incorporate a wide range of perspectives on animal use, and give appropriate weight to animal welfare concerns.

❖ Industry

The pharmaceutical, chemical and other industries are responsible for a significant proportion of animal use around the world, since the development and safety assessment of their products usually relies heavily on the results of animal tests. This, and the fact that these industries make a lot of money from the products they manufacture, means that there is a clear onus on those involved to develop high standards of animal care and use and to implement the 3Rs. Furthermore, since most companies are multinational, they are well placed to harmonise standards in their facilities around the globe.

As with the funding bodies, industry generally argues that the research it does is in the public's name, contributing to health and safety. However, industry also needs to take into account public concern for the suffering of animals. Openness and transparency about animal use is very important. This is already recognised by some companies who publish considerable information on the species and numbers of animals they use (e.g. Novo Nordisk 2006) as part of their Corporate Social Responsibility Policy. This contributes to public understanding and helps inform the ethical debate about animal use in science.

There is also considerable scope for individual companies to reduce the harms to animals and make significant and immediate improvements in animal welfare throughout the whole lifetime experience².

Industry is also in a strong position to challenge the traditional requirements of regulatory authorities, or wordings of test guideline programmes. Adopting a challenging and innovative approach to the development and implementation of humane alternatives and having a company-wide strategy to achieve significant advances in this respect, demonstrates real commitment to addressing concerns about animal use.

Multinational companies should develop and implement universal standards of good practice with respect to all of these issues, using those in their most progressive facilities as the benchmark. It is unacceptable to intentionally undertake animal tests in countries where legislative requirements and animal welfare controls are less stringent. Companies should also actively encourage the wider dissemination of 'best practice' standards (rather than simply citing 'commercial sensitivity' as a blanket reason to avoid doing so). Being prepared to include animal behaviour and welfare specialists in discussions on these kind of issues, including those from animal welfare organisations, would be a welcome move that

would bring different expertise and perspectives to the table.

❖ **Regulatory authorities**

There is considerable opportunity for considering ethical, 3Rs and animal welfare issues in the development and administration of the regulatory requirements that involve tests on animals. These requirements are responsible for a significant amount of animal use. For example, 86% of all the toxicological procedures conducted in the UK during 2006 were performed 'to conform to legal or regulatory requirements' (Home Office 2007). These requirements are used as the justification for such animal use - however, regulatory requirements also have the potential to act as a framework within which to advance other aspects of animal welfare such as the implementation of humane alternatives, improvements in husbandry and care and the refinement of procedures.

Regulatory authorities, whilst acting to protect the health of humans, other animals and the environment, must accept the desirability of replacing animals with alternative methods, both from an ethical and scientific standpoint. The organisations involved include those who establish the regulatory requirement for risk or hazard assessment data to be generated (legislators e.g. national governments, the European Commission), those who interpret the legislation to set out in detail the type of data required (regulators such as the European Medicines Evaluation Agency), and those who seek to establish and/or harmonise testing methods and strategies (e.g. the OECD, ICH). All have a responsibility to critically consider the animal welfare and ethical aspects of their activities and all should collaborate with regard to the issues below.

Regulatory authorities should consult widely (and liaise closely with similar bodies in other trade blocs or regulatory regions) to ensure that positive developments in the 3Rs are incorporated quickly and widely into test guidelines and/or regulations. Successfully validated alternative methods are sometimes not accepted by all regulators (or only conditionally) and then only after a number of years of discussion. Such long delays are clearly unacceptable. A clear procedure for the development, validation and acceptance of promising new alternative methods (whether completely replacing the use of animals or using a method that causes less suffering) should be identifiable and adhered to.

There must be flexibility with regard to regulatory requirements in the way in which acceptable test data may be generated, with scope for avoiding or at least minimising the use and suffering of animals. Currently, and in many cases, specific test requirements allow for little flexibility e.g. in the

species to be used and the housing environments of test animals.

In many instances, the way in which the laws relating to assessing the safety of substances (e.g. chemicals, new pharmaceutical products) are interpreted into test guidelines by regulatory bodies, will have a direct impact on the numbers of animals used and how much they suffer. For example, the impact on animals may be reduced where a 'step-by-step' testing process is advocated rather than doing all proposed animal tests simultaneously.

Given that animal models are variable in their ability to accurately predict risk, there should also be a transparent mechanism available for waiving specific regulatory requirements in cases where sound arguments, supported by evidence, can be put forward to demonstrate that an animal test is either unnecessary or will not serve the purpose of the legislation. Animal tests should certainly *not* be done if it is uncertain that the information they produce will be of value and lead to effective action to minimise risks to humans, other animals and the environment.

❖ **Education and training**

Scientific endeavour does not take place in a moral vacuum. Scientists undertake their work within a legislative and ethical framework influenced by prevailing societal attitudes which in turn are affected by concern generated by particular research directions, rapid developments in technology (e.g. genetic engineering and stem cell technology) and increasing understanding of animals and their ability to suffer. Education and training has an important role to play in developing an individual's knowledge and understanding of ethical and animal welfare issues.

The UK's Quality Assurance Agency for Higher Education (2002) has stated that it is important for students in the biosciences "*to be confronted by some of the scientific, moral and ethical questions raised by their study discipline, to consider viewpoints other than their own, and to engage in critical assessment and intellectual argument*". The use of animals in research and testing is a key issue for such debate. It provides a significant opportunity for students to be introduced to the concept of ethical review and to develop their own critical thinking in relation to the use of animals in science, and how they would act in their future careers with respect to animals and their welfare.

A rounded education should encourage students to discuss, understand and begin working towards proficiency in the ethical, scientific and practical animal welfare aspects of a career in the biosciences. It is important for them to be introduced to the spectrum of views in society on the use of animals in experiments, and to understand the legitimate concerns held by many people, rather than to be

exposed only to those at either end of the spectrum.

Understanding the link between good science and animal welfare is also essential. Poorly designed experiments, and those that cause animals to suffer physiologically or psychologically, will invariably not deliver reliable or reproducible results, so training future scientists in good experimental design is also very important. In addition, students need to gain sufficient understanding of the behaviours and needs of animals, and of their capacity to suffer, such that they fully appreciate that animals are not simply 'research tools', but are individual sentient beings each capable of experiencing pain, suffering and distress. Their training should encourage them to always think beyond the status quo and the use of traditional methods, and to actively seek ways of implementing all 3Rs in whichever field of science they enter.

The importance of specific and mandatory training for those who care for and/or use animals has been described elsewhere (see APC 2006, FELASA 2001) as has the importance of Continuous Professional Development schemes. Provision of training opportunities - both formal and informal - is vital to ensure all relevant personnel are kept fully informed of developments in the 3Rs, and those relevant to animal welfare and thinking around the ethical issues.

❖ Scientific journals

With increased focus on ethical issues in science, so the roles and responsibilities that scientific journals have when reviewing the research they publish has become more important. For this reason, journals need to acknowledge the importance of publishing a clear ethical statement regarding the nature of the animal research that they are prepared to publish.

Through such editorial policies, journals also have a significant opportunity to influence how scientific research is conducted. Journals are in an ideal position to publish and thus more widely disseminate information relating to the 3Rs and animal welfare and should be more proactive in encouraging the submission and publication of such information within papers. By publishing research in sufficient detail (including specific information on species, animal numbers, housing and husbandry standards, how pain, suffering and distress were minimised, humane endpoints and methods of euthanasia) the methods can be critically examined and refinements disseminated. Information on adverse effects of the experimental procedures on animals and the steps taken to reduce these (important for scientific as well as ethical reasons) allows other scientists in the field to identify novel refinements used, or else highlight scope where refinements could and should be pursued. This information can also be used to inform future ethical review processes and harm/benefit analyses

which will increase the rate at which information is disseminated, so acting as a driving force to improve animal welfare and scientific standards around the world.

Conclusion

A wide range of opportunities exists for critically assessing the ethical and animal welfare aspects of the use of animals in research and testing. Some are already being implemented in some countries around the world, but in most cases, far greater commitment is required in order to realise the benefits that developing these opportunities would bring to animal welfare and science.

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Footnotes

1. For example, at an international level, the Member States of the European Union agreed it was no longer acceptable to use animals to test cosmetics ingredients or products, and agreed to ban such testing and the sale of such products across Europe, by 2013 (European Commission 2003). At a national level, the UK has declared that licenses will not be issued to use animals in programmes of work for the development or testing of offensive weapons, alcohol or tobacco products (Home Office 2000). With regard to the species to be protected, the European Directive and national legislation within the EU covers all vertebrates, but some individual countries such as the UK also includes one species of invertebrate, *Octopus vulgaris* (Home Office 2000). The use of great apes in scientific procedures with the potential to cause pain, suffering, distress or lasting harm is considered unacceptable and is therefore not allowed in New Zealand, Netherlands, Sweden, UK or Austria.
2. For example, by providing animals with a good quality of life by investing significant resources in housing and care; continuously reviewing and refining experimental procedures to minimise suffering; establishing limits on the level and duration of animal suffering permitted (e.g. not undertaking any work involving substantial suffering); minimising wastage of animals in-house and through co-ordination with breeders; developing rehoming strategies for animals; investing significant resources in staff training where appropriate.

