

Using animals in research, testing and teaching

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Summary

The authors describe landmarks in animal-based research and examine key moral statements on the use of animals in scientific research. The principles of '*reduction, replacement and refinement*' are suggested as a focus around which both the animal welfare and the scientific communities of the world can unite. This paper reviews the progress achieved in the *replacement* of animal use by non-animal methods, with a focus on regulatory testing. In addition, it presents evidence of a *reduction* in the numbers of animals used throughout the 1990s. The authors also emphasise the need for concerted efforts to contain a potential escalation in these figures, resulting from current inefficiencies in creating genetically modified animals and increasing demands for regulatory testing. Finally, the authors examine the *refinement* of techniques to mitigate and prevent pain and distress, with an emphasis on appropriate endpoints as an effective tool. They present the need for the international harmonisation of ethical standards and processes, together with a suggested harmonisation platform, and demonstrate the central role that should be played by the institutional Animal Care Committees.

Keywords

Alternative – Animal Care Committee – Animal testing – Animal welfare – Biotechnology – Ethical review process – Ethics – Genetically modified animals – Harmonisation – International standard – Non-animal method – Reduction – Refinement – Regulatory testing – Replacement.

Introduction

At the start of the twenty-first century, it is obvious to the public, as well as to the scientific community, that science often raises a number of ethical questions. In the areas of animal-based research, testing and teaching, these include questions about the justification for studies involving pain and distress, which are obviously detrimental to animal welfare. Determining the social and behavioural needs of an animal and deciding how these needs can best be met are further concerns, arising from the fields of animal welfare science and behavioural biology, which should inform the debate about the use of animals. Furthermore, recent scientific advances in biotechnology raise a new and significant series of questions about the acceptability of modifying the genome of an animal.

Landmarks in animal-based research and key moral statements

The research into and testing of almost every major medical treatment has involved the use of animals at some stage (36). However, for as long as animals have been used to better understand the workings of the human/animal body, the general public and thoughtful researchers have also concerned themselves with issues arising from that use. In particular, the question of pain and distress has been the main focus of concern.

During the seventeenth century, as William Harvey was demonstrating the value of comparative physiological

investigation in illustrating the circulation of the blood, three other professional physiologists, Robert Boyle, Robert Hook and Richard Lower, were the first people to record their genuine concern for the welfare of their experimental subjects. This concern was based on the moral objection of these physiologists to perceived animal cruelty. In the eighteenth century, the English utilitarian philosopher, Jeremy Bentham, focused attention on concern for animals based on their capacity to suffer. Physiologist Marshall Hall pioneered the consideration of welfare issues from within science by proposing that physiological procedures should be regulated to take into account the suffering of animals (50).

In the nineteenth century, work on the anaesthetic properties of ether led to sophisticated surgical procedures and greater use of animals. As the use of anaesthetics enabled experiments to be performed with minimal suffering, the United Kingdom (UK) Royal Society for the Prevention of Cruelty to Animals changed its position from outright objection to the use of animals for scientific procedures to objecting to painful procedures on animals. In the same period, the British Association for the Advancement of Science published guidelines aimed at minimising suffering and discouraging the conduct of experiments of dubious scientific merit, and the UK 'Cruelty to Animals Act' was passed.

With World War I, the focus on antivivisection shifted; benefits to human health through animal research were welcomed by the public, particularly by those who had witnessed human suffering as a result of the war (48). On the other hand, in the wake of harmful experiments on human subjects during World War II, many scientists found it necessary to reconsider their post-war roles to incorporate both the empirical and the ethical issues inherent to science. The 1970s and 1980s saw increased debate about the use of animals among moral philosophers. Works addressing this concern were published by Australian philosopher Peter Singer (*Animal Liberation*) (49), Richard Ryder (*Victims of Science*) (47) and Tom Regan (*The Case for Animal Rights*) (40). Since these publications were accessible to the lay public, and were firmly rooted in ethical theory, they attracted the attention of opponents of animal research as well as academic philosophers. Further information on the chronology of landmarks in animal-based research and key moral statements will be found at <http://www.ccac.ca/english/educat/edframe.htm>; http://www.rdonline.org.uk/pages/home.asp?i_ToolbarID=8&i_PageID=94; <http://www.amprogress.org/Issues/issuesmain.cfm> and in Monamy (32).

In general, studies that have explored public acceptance of using animals in research have found that approximately 85% of the population support the use of animals for research, provided that there is stringent oversight of that use and that pain and distress are minimised (31).

However, Gott and Monamy (27) describe surveys conducted in greater Europe, the UK, New Zealand and the United States of America (USA) which indicate that approximately 70% of respondents are against the genetic modification of animals. This may be the result of general confusion about the issues raised by genetic engineering, and there is some evidence that, when specific uses are discussed with the public, there is greater acceptance of genetic engineering for specific purposes (15, 23). However, there are doubtless deeply rooted concerns about the novel use of animals, particularly since potential benefits have yet to be widely experienced (27).

Moral stewardship

At present, there is no widely accepted comprehensive moral theory on research involving laboratory animals. In the absence of a universal ethic of animal experimentation, those concerned with animal welfare, both scientists and non-scientists, have plotted a different course of action, recognising that animal researchers have a role to play as moral stewards of their research subjects. To a certain extent, this view can be said to be based on the approach of Albert Schweitzer (1875-1965), Nobel Peace Laureate, medical practitioner and doctor of philosophy: i.e. to cause pain or death when it can be avoided is wrong. In this context, animal experimentation is viewed as a 'necessary evil', which is justifiable as long as those who conduct the experiments accept their moral obligations, both to society and to the animals in their care (32). This is the convergence point for scientists, veterinarians, animal care technicians, students, community representatives and representatives of animal welfare organisations, all of whom participate in the various national legislated or voluntary systems of ethical review for the care and use of animals involved in scientific studies.

In a number of systems that oversee animal use, ethical decisions are based on a form of cost-benefit analysis (50). In essence, the potential benefits to be obtained from the research are evaluated against the costs to the animals, generally in terms of pain and/or distress (7). Only then is it decided whether the animal-based study should proceed. The interest in creating genetically modified animals to use as models for biomedical research, as well as for other purposes, such as producing pharmaceuticals or as an improved food source, has led to a re-examination of the ethical basis for animal use. In a seminal report on the ethical implications of emerging technologies for breeding farm animals, Banner (5) recognised that the cost-benefit analysis could not be the sole test of ethical acceptability. In fact, there are a range of potential intrinsic ethical objections that must be considered; for example, whether genetic modifications that change the essential nature of an animal (6, 44, 56) should be permitted. These concerns are quite distinct from other 'extrinsic' factors, such as whether a particular genetic modification of an

animal could pose a risk to the environment, human health or the welfare of the animal itself.

Ethical principles: reduction, replacement, refinement

In 1957, the Universities Federation for Animal Welfare commissioned the text of *The Principles of Humane Experimental Technique* (46). The work of Russell and Burch pioneered the tenets of 'reduction, replacement, refinement' (the 'Three Rs'), which have become a uniting focus for both the animal welfare and scientific communities worldwide, over the past forty years. Adherence to the Three Rs is now a requirement of most if not all legislated and self-regulated national systems of surveillance.

The evolution of the Three Rs concept has been described by Balls *et al.* (4). It is important to note that, collectively, the Three Rs have been termed 'alternatives', following the 1978 publication of *Alternatives to Animal Experiments* (51) by David Smyth, a physiologist and President of the UK Research Defence Society. In this book, Smyth provides a definition of alternatives as: 'all procedures which can completely replace the need for animal experiments, reduce the numbers of animals required, or diminish the amount of pain or distress suffered by animals in meeting the essential needs of man and other animals'. Further information on defining and satisfying the ethical principles for research, teaching and testing can be found at the following website addresses:

- <http://www.ccac.ca/english/educat/edframe.htm>
- <http://www.frame.org.uk>
- <http://www.animaethics.org.au/reader/arrp-3rs>.

The Three Rs focus primarily on laboratory animal use. Their premise is that, by replacing, reducing and refining animal use, the costs to animal life are minimised, while the benefits (usually to humans) are maximised. However, there are some types of research which may require a different approach. For example, the emerging field of animal welfare science is providing important information which will benefit animals themselves. These benefits may include improvements in housing systems for production animals or species used in laboratory-based studies. In addition, the current interest in pain perception in fish may influence the manner in which fish are treated, both in the laboratory and on fish farms (16). Albrecht (1) debated that some uses of animals, in particular, wildlife research, where the pain and distress inflicted on an individual animal may lead to improved conservation outcomes for the species as a whole, require a new way of determining what constitutes the 'ethical use' of such animals.

National surveillance systems for the use of animals in science

Although the various national systems of overseeing the care and use of animals may appear to be quite diverse in operation, they have many fundamental elements in common. They all involve laws, regulations, guidelines and/or policies which affect the worksite, the work programme, the personnel and the training requirements for key staff. Authorisation may be invested centrally (as in the UK), regionally (as in several European countries) or locally, through institutional Animal Care Committees (ACCs), as in Canada, the USA and Australia.

Canada is recognised (38) as having pioneered the establishment of ACCs as the keystone of peer-based ethical review processes and local quality control. An ACC should represent a microcosm of society, including representatives from the public and animal welfare movement, in addition to veterinarians, scientists, animal care staff and students. At the national level, the Canadian Council on Animal Care (CCAC) provides quality assurance for institutional animal care and use, through its peer-based evaluation programme, which includes monitoring ACC functions. However, while ethical review processes performed mostly through ACCs have become the norm worldwide, several countries still lack quality assurance mechanisms, in the form of certification or accreditation programmes, to verify that an institution has fulfilled its national requirements.

Further information on comparisons between national surveillance programmes for overseeing animal use and national ethical standards were presented at a 2003 International Workshop on the Development of Science-based Guidelines for Laboratory Animal Care (34). At this workshop, adoption of the Canadian system was recommended for those countries that do not already have a surveillance system in place (34). Information on the CCAC can be found at <http://www.ccac.ca>.

Ethical issues

Replacement

Replacement often means replacing the use of animals with an inanimate system (e.g. substituting a computer model or program, or a mannequin on which medical procedures can be practised). It can also mean the replacement of sentient animals (usually vertebrates) with less sentient animals (usually invertebrates, such as worms, bacteria, etc.). Replacement also includes the use of cell and tissue cultures, usually derived from animals.

Most national systems of oversight require that animals should only be used when no other method is available to meet the scientific aims of the study. The replacement of animals in research has occurred mainly through improvements in techniques which enable scientists to look for mechanisms of action at the cellular and molecular levels, rather than using a 'whole animal' approach. More focused attempts to replace animal use have been made in the areas of teaching and testing. The ethical issues involved in the use of animals to demonstrate already known facts have encouraged the development of a substantial body of non-animal models for teaching purposes (<http://www.eurca.org/>; <http://oslovet.veths.no/NORINA>; <http://www.lawte.org/exchange/walshaw/walshaw.html>).

In the area of regulatory testing, concerted efforts have been made to develop non-animal methods, since testing by its nature involves the deliberate infliction of pain and distress on an animal, and because tests require specific endpoints, which are easier to model in a non-animal context or 'set-up'. Despite the development of considerable numbers of *in vitro* tests, very few are actually currently used for regulatory purposes. For a new test to be accepted by a regulatory agency, it must undergo a complex validation process (3). Criteria for a validation study have been developed through the collaboration of the Organisation for Economic Co-operation and Development (OECD) (http://www.oecd.org/document/30/0,2340,en_2649_34365_1916638_1_1_1_1,00.html), the European Centre for the Validation of Alternative Methods (ECVAM) (<http://ecvam.jrc.it/index.htm>) and the Interagency Coordinating Committee for the Validation of Alternative Methods (ICCVAM) (<http://iccvam.niehs.nih.gov/>). The organisations ECVAM and ICCVAM also work to ensure that tests which have been validated are peer-reviewed and that their use is recommended to relevant regulatory authorities.

Nonetheless, hurdles to the acceptance of *in vitro* methods for regulatory testing remain. Often, the animal test against which the *in vitro* data are to be evaluated has itself never been validated (2), leading to difficulties in interpreting data. In addition, regulatory agencies, which bear the responsibility for protecting human, animal and environmental health, tend to be conservative in adopting new approaches.

Reduction: decreasing the numbers of animals used for scientific purposes

Orlans (39) reported the number of laboratory animals used in research in 24 countries, spread over four continents, in the late 1990s as a total of 28,025,000. A more recent report by the Nuffield Council on Bioethics (36) estimated that up to 50 million animals are used in research every year worldwide. The total number of

animals used has been the parameter employed most frequently to examine both long-term and emerging trends and to compare the effectiveness of various countries in implementing the Three Rs.

Since the UK has the strictest system of regulation of animal research (36), it is often used as a reference point. Rowan *et al.* (45) reported that there is plenty of evidence to indicate that the major fall in animal use observed in the UK during the 1970s and 1980s, due to more targeted approaches involving *in vitro* screening of chemicals by the pharmaceutical, chemical products and cosmetic industries, also occurred in Europe, the USA and Japan. However, a statistical trend analysis study (25) using original data on animal use, published between 1980 and 1999 by the UK Home Office, the US Department of Agriculture and the CCAC, indicated that the total number of animals used in the USA and Canada did not show any downward or upward trend through the 1980s. This was probably due to the much lower ratio of research and testing conducted in these countries by commercial (pharmaceutical and cosmetic industry) as opposed to public (academic institutions) and government laboratories. This ratio was estimated to be approximately 22 (commercial):65 (academic):13 (government) in Canada and 40:30:30 in the USA, compared to 60:20:20 in the UK.

A sustained downward trend of similar magnitude occurred in the UK, USA and Canada throughout the 1990s, demonstrating their equivalent effectiveness in implementing reduction measures during this period. This is interesting in view of the fact that, whereas the UK surveillance process is legislated, Canada has evolved a non-legislative system, since animal welfare there is not a federal but a provincial jurisdiction. The USA has evolved a hybrid system, involving both legislation and voluntary compliance, an approach also adopted by several countries in Europe and Asia.

Although the number of animals used globally appears to have stabilised in recent years, there are predictions that, by 2005, the total number of research animals will begin to increase, reflecting the upsurge in research involving genetically modified animals (42). A Medline search of published papers referring to the use of genetically modified animals showed a consistent increase in the use of these animals over the past 13 years (Fig. 1). National surveillance bodies will need to make a concerted effort to address current inefficiencies in the creation of genetically modified animals if an escalation in numbers is to be avoided (10).

In addition, there are increasing demands for the use of animals in regulatory tests; for example, to address the gaps in knowledge of the toxic effects of chemicals produced in high volume (<http://www.epa.gov/chemrtk/>

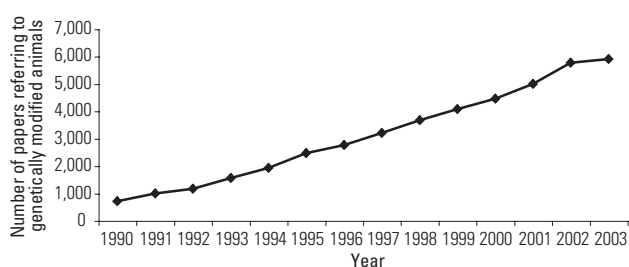


Fig. 1
Trends in the use of genetically modified animals between 1990 and 2003, as determined by a Medline search conducted in November 2004

volchall.htm) and the effects of endocrine disruptors on human and environmental health (54). Considerable use of animals can be avoided if regulatory agencies adopt emerging techniques, e.g. proteomics and toxicogenomics as screening tools, rather than placing sole reliance on animal-based tests (17). The incorporation of *in vitro* methods into a tiered testing strategy, based on sound science, is an approach that has been used to good effect in eye irritation testing (18, 53).

In general, improvements to the design of animal experiments (21), as well as appropriate statistical techniques (20), will lead to the use of fewer animals and more valid data.

Refinement: mitigating and preventing pain and distress

Refinement has been viewed as the least 'exciting' of the Three Rs, since it produces the least obvious change in animal use, if numbers are regarded as the most important measuring tool. Nonetheless, Russell and Burch placed a greater emphasis on minimising pain and distress to the individual animal, rather than on reducing the numbers of animals in general (46). They recognised that the welfare cost to animals used for scientific purposes has two components, as follows:

- the direct costs of the procedures used
- 'contingent costs', which include housing and husbandry.

The refinement of techniques has a significant role to play in both the reduction and replacement of animals in research, teaching and testing. Using these techniques will result in less variability and improve the results obtained. This, in turn, has the potential to minimise pain and distress to the animals involved. For example, introducing new and safer anaesthetic agents, together with better training of investigators in their use, has reduced the number of anaesthetic deaths. Pain in laboratory animals is

a major animal welfare problem that must be addressed. Increased efforts in the recognition of pain and distress in laboratory animals has led to research on improving analgesics to help mitigate the adverse effects of procedures (22, 33). The refinement of husbandry, particularly by increasing the complexity of social and physical environments, has improved the wellbeing of research animals without compromising experimental results (57). In addition, Reinhardt (41), among others, has pointed to the importance of a positive human-animal relationship in research laboratories. A positive relationship between the caregiver or researcher and the animal may result in an overall reduction of stress for that animal, and may also help to buffer the potential stress of certain experimental procedures. Training laboratory animals to accept routine procedures is also an important means of reducing animal and personnel stress.

In general, refinement of animal use is also achieved by training animal users. This is becoming a prerequisite for obtaining approval for animal experiments in a number of countries. The Federation of European Laboratory Animal Science Associations (FELASA) was instrumental in developing recommendations for training various categories of animal users (<http://www.felasa.org/recommendations.htm>). More recently, the CCAC has published guidelines outlining the requirements for an institutional animal user training programme (14).

In 2001, the OECD deleted the classical lethal dose 50 (LD₅₀) test (Tg401) from its test guidelines series. It was replaced with three alternative methods, Tgs 420, 423 and 425, which are designed to use fewer animals and to reduce the levels of pain and distress. They achieve this by specifying rules that determine when procedures should be stopped and requiring adherence to the OECD guidance document on humane endpoints (see below). The withdrawal of Tg401 was a lengthy process, and provides an example of the commitment needed by regulatory agencies and supra-national bodies to improve both animal welfare and the scientific validity of regulatory tests (8).

In biotechnology, one of the key difficulties in ensuring the well-being of genetically modified animals has been the potential for unanticipated pain and distress that can arise from the procedures involved in their creation. For example, random integration of a transgene into the genome of an animal may result in a detrimental phenotype. Thus, it is important that research workers give careful attention to the potential for pain and distress (11), and that any new strain is carefully monitored for signs of compromised welfare (29). Cloning may be used in conjunction with genetic modification technology. However, it differs considerably, in that a clone is an organism or cell derived from a single ancestor by asexual means. There are welfare concerns currently associated with cloning technology, in particular, larger than normal

birth weights. These can lead to birthing complications; in addition, the offspring may develop respiratory problems later in life, as well as immune system deficiencies (19).

Regulatory testing and invasive studies: appropriate endpoints as an internationally recognised effective refinement tool

Refinement has its greatest impact on the reduction of pain and distress to animals. In the past, for invasive studies involving vaccine testing, infectious diseases, tumours, organ rejection, toxicity testing, etc., the endpoint for the animal may have been death. As an animal approaches death, it stops eating and drinking and rapidly becomes dehydrated. Except for a small number of instances, death can be predicted to occur within a short period of time from the point at which the animal stops eating and drinking. Pilot studies should be conducted to determine which clinical signs are most useful in ensuring that the endpoint has been reached. In this way, the experiment can be terminated at the earliest point at which the scientific goals are reached before the animals suffer needlessly. For an overview of humane endpoints in animal experiments for biomedical research, see Hendriksen and Morton (28).

Canada was the first country to develop and implement guidelines on endpoints. In 1998, the CCAC guidelines on choosing an appropriate endpoint in experiments using animals for research, teaching and testing (12) were published in French and English. A Spanish version was published by *Animales de Experimentación* in 2000 (13). This document was recognised as an effective refinement tool, along with the OECD *Guidance Document on the Recognition, Assessment and Use of Clinical Signs as Humane Endpoints for Experimental Animals Used in Safety Evaluation* (37), at the Third World Congress on Alternatives and Use of Animals in Life Sciences in 1999. Unlike the CCAC guidelines, the OECD guidance document addresses the principles of humane experimentation for animals used in toxicity testing studies only.

These guidelines on endpoints emerged as a flexible basis for worldwide harmonisation at the June 2001 International Symposium on Regulatory Testing and Animal Welfare, organised by the CCAC in collaboration with the International Council for Laboratory Animal Science (ICLAS). Building on the continuing efforts of the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and the OECD, this symposium brought representatives of the regulatory agencies involved with evaluating pharmaceuticals, biologicals and chemicals for safety and efficacy from twenty-two countries together for the first time. Also present were representatives from national research agencies, universities, industry and animal welfare groups. The objectives of the symposium were to identify best practices and promote improved welfare for animals

used in regulatory testing. The Proceedings of the ICLAS/CCAC International Symposium on Regulatory Testing and Animal Welfare (35), published by the USA National Research Council, represent a valuable international resource, detailing recommendations on current best scientific practices as well as suggestions on future improvements and their implementation within the regulatory environment.

International harmonisation of standards for the care and use of animals in science as a priority

Gauthier and Griffin (26) have pointed to the need for international harmonisation of standards as a priority for the following reasons:

- there are broad implications for international scientific collaboration
- it will aid global acceptance of research data
- it will facilitate international trade.

International harmonisation platforms

In parallel with the development of biomedical research, laboratory animal science and service organisations have been in constant evolution over the past forty years. Demands for 'higher quality' animals (i.e. animals which are healthier or have other relevant characteristics, such as a defined genetic background), together with a greater concern for animal welfare, are the driving forces behind the development of organisations that provide support for people working in the field of laboratory animal science. A useful overview of the principal laboratory animal science organisations around the world, according to their primary aims and scope (i.e. international organisations, laboratory animal science associations, professional organisations and animal care and welfare organisations), can be found in Vergara and Demers (55).

Several organisations could facilitate the harmonisation of standards at the international level, such as the OECD, ICH, World Organisation for Animal Health (OIE), the Institute for Laboratory Animal Research (ILAR) and ICLAS. For example, ICLAS has already made important advances in harmonisation, particularly over the past five years, through the following conferences:

- the 2001 ICLAS/CCAC International Symposium on Regulatory Testing and Animal Welfare
- the 2002 American Association for Laboratory Animal Science (AALAS)-ICLAS Summit of the Americas

- the 2003 ILAR-ICLAS International Workshop on Harmonization
- the 2004 FELASA-ICLAS Symposium/ Meeting on Harmonization.

Moreover, and equally importantly, the OIE held a global conference on animal welfare in February 2004 (<http://animal-welfare.oie.int>), to promote the development of internationally agreed science-based animal welfare standards.

The central role of the institutional Animal Care Committees

While an effective platform or forum is a key element of the harmonisation process at the international level, the keystone of the whole enterprise remains the local, institutional ACCs, also called 'institutional animal care and use committees' or 'ethical review processes'. After thoroughly reviewing the best scientific practices for supervising ACCs and animal use, participants in the ICLAS/CCAC International Symposium on Regulatory Testing and Animal Welfare stated: 'Experience has shown that different frameworks (voluntary or legislated) provide effective oversight in different jurisdictions and with organisations with different cultures. Indeed, providing the process works in practice, diversity, which can of itself promote continuous improvement, should not be discouraged. Future progress requires the following: encouraging diversity; networking ACCs to identify, encourage and share best practices' (43).

International harmonisation of standards is what is needed, not international standardisation. The institutional ACC has a central role to play in this process for the following reasons:

- it is representative of the scientific culture and moral values of its home country
- it aids communication and enables informed decision-making at the local level
- it is already integrated, as an accountable keystone, into most national oversight and regulatory systems worldwide
- it provides each country with an enhanced ability to influence the international harmonisation of best practices for animal care and use in science (24).

Conclusion: summary of policy directions

Ethical issues

Questions concerning the use of animals in research, testing and teaching will continue to be asked, particularly

in areas where the pace of technological change is rapid. Answers to these questions must take into account scientific validity, accepted community beliefs about animals and their relationship with humans, and the interests of the animals themselves.

National surveillance

The ACC, which includes researchers, veterinarians, animal care technicians, community representatives and animal welfare representatives, can provide a broad spectrum of community views on the use of animals on a practical, case-by-case basis (27). However, there must also be some form of national surveillance mechanism to provide quality assurance for local processes. This involves the establishment of policies and principles that take into account the national culture, while also considering the harmonisation of key principles with those of other national authorities.

Numbers of animals

While significant progress has been made in reducing the numbers of animals used for research, teaching and testing, there is now the likelihood that, within the next few years, the numbers will increase once more. This is due to public concerns about the impact of chemicals on human health and the environment and the ability to selectively target the components of an animal genome. Public policy must be carefully examined in the future to ensure that the best scientific practices are employed, including good experimental design and analysis, to assure the public that animal lives are used only when other means are not available.

Regulatory testing

In the area of regulatory testing, differences in national and international test guidelines are unacceptable from both scientific and animal welfare points of view, as well as for economic reasons, since unnecessary or repeated testing places a financial burden on companies that operate at an international level (52). Standardisation can be a lengthy process, as evidenced by the long route to withdraw the requirement for the LD₅₀ test. However, the gains made in minimising animal use can be substantial (30).

Animal welfare has only relatively recently become a concern for regulatory authorities. Thus, the development of testing protocols to satisfy regulatory requirements may not have involved laboratory animal specialists. In future, it will be important to ensure that animal-based tests are based on sound scientific principles and best animal welfare practices. As demonstrated at the 2001 ICLAS/CCAC Symposium on Regulatory Testing and

Animal Welfare, best practice in regulatory testing requires constructive debate among those who develop and implement regulatory requirements, those who conduct animal testing and those national bodies responsible for the regulation of animal use (43).

Genetically modified animals

Some countries have developed specific guidelines for the creation and use of genetically modified animals (11) (http://www.homeoffice.gov.uk/docs/sub_transgenic.html). For the most part, these guidelines focus on external factors that may:

- minimise pain and distress
- prevent these animals escaping into the environment

– prevent by-products from entering the animal or human food chains.

Since the use of genetically modified animals is increasing, it will also be important to address other 'intrinsic factors'; for example, to determine to what extent human ends and purposes should be permitted to override the essential nature of a particular species (6). Such discussions are beginning to occur in the literature (9, 27), and attempts have been made to engage the broader public in debate (15, 23, 36). The policy that results from these discussions will be a crucial element in the ethical use of these new technologies.

L'utilisation des animaux pour les besoins de la recherche, des essais et de l'enseignement

C. Gauthier & G. Griffin

Résumé

Les auteurs décrivent les repères chronologiques qui jalonnent la recherche sur les animaux et examinent les principales prises de position morales relatives à l'utilisation des animaux pour les besoins de la recherche scientifique. Les principes de « *réduction, remplacement et raffinement* » sont proposés comme thème central autour duquel les milieux scientifiques et les défenseurs du bien-être animal dans le monde peuvent se rejoindre.

Le présent article examine les progrès accomplis en matière de *remplacement* de l'utilisation des animaux par des méthodes substitutives, en mettant l'accent sur les tests réglementaires. En outre, il apporte la preuve de la *réduction* du nombre d'animaux utilisés durant les années 1990. Les auteurs soulignent également la nécessité de déployer des efforts concertés pour empêcher une augmentation possible de ce nombre résultant des facteurs d'inefficacité actuels en matière de création d'animaux génétiquement modifiés et de la demande croissante d'essais réglementaires.

Enfin, les auteurs examinent le *raffinement* des techniques pour atténuer et prévenir la douleur et la détresse, en mettant l'accent sur les points limites appropriés en tant qu'outil efficace. Ils expliquent la nécessité d'une harmonisation internationale des processus et des normes éthiques, proposent une base sur laquelle fonder cette harmonisation et démontrent le rôle central qui devrait être joué par les Comités institutionnels de protection des animaux.

Mots-clés

Alternative – Animal génétiquement modifié – Bien-être animal – Biotechnologie – Comité de protection des animaux – Essai sur les animaux – Éthique – Harmonisation – Méthode alternative à l'utilisation des animaux – Norme internationale – Processus de révision éthique – Raffinement – Réduction – Remplacement – Test réglementaire.

El uso de animales en la investigación, la experimentación y la enseñanza

C. Gauthier & G. Griffin

Resumen

Los autores describen puntos principales en la investigación basada en el uso de animales y examinan los principios morales básicos sobre el uso de animales en la investigación científica. Los principios de "reducción, reemplazo y refinamiento" son sugeridos como un punto de referencia en el que se podrían reconciliar a los grupos que protegen el bienestar de los animales y a los intereses de la comunidad científica mundial.

Este trabajo hace un resumen del progreso alcanzado por el reemplazo en el uso de animales por otros métodos que no usan animales, con referencia especial a las pruebas reglamentarias obligatorias. Además, se presenta evidencia de que hubo una reducción en el número de animales que se usaron a través de la década de 1990. Los autores enfatizan la necesidad de un esfuerzo concertado para frenar un posible aumento de estas cifras, como resultado de la falta de técnicas eficientes para crear animales genéticamente modificados y la demanda creciente de animales requeridos para pruebas reglamentarias obligatorias.

Finalmente, los autores examinan el refinamiento de las técnicas para mitigar y prevenir el dolor y la angustia, enfatizando en la selección de puntos finales como una herramienta muy efectiva en este proceso. Ellos exponen la necesidad de armonizar a escala internacional los procesos y las normas éticas, al mismo tiempo sugieren una plataforma de armonización y demuestran el rol central que deberían desempeñar los comités institucionales de protección de los animales.

Palabras clave

Alternativa – Animal genéticamente modificados – Armonización – Bienestar de los animales – Biotecnología – Comité de protección de los animales – Ética – Método sin usar animales – Norma internacional – Proceso de revisión ético – Prueba reglamentaria obligatoria – Prueba usando animales – Reducción – Reemplazo – Refinamiento.



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