

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 Laboratory Animals Veterinary Association, UK

Q1. WHAT IS YOUR VIEW ABOUT THE USE OF ANIMALS IN RESEARCH?

The Laboratory Animal Veterinary Association (LAVA) broadly comprises veterinary surgeons with a keen interest in the welfare and care of laboratory animals. Many of our members are employed as Named Veterinary Surgeons at research establishments; others are veterinary surgeons engaged in research and who may need to use animals for all or part of their research programme. Council will appreciate that for veterinary surgeons, trained in the diagnosis and treatment of animal diseases and having a sense of responsibility for the welfare and care of all animals, the use of animals in research creates something of an ethical dilemma. Fundamentally, we wish to see a situation develop where the use of animals in science becomes unnecessary. We recognise, nevertheless, that veterinary surgeons use the products of this research, animal vaccines, medicines and surgical procedures, as part of their daily routine for the treatment or prevention of disease in animals. As members of a caring veterinary profession that prides itself on being held in high esteem by a demanding public, we adopt a proactive attitude towards the prevention of suffering and disease in animals and in their humane care and protection. We believe, therefore, that we have a duty to become actively involved in the use of animals for scientific purposes.

Information Provided by Research

There is, no doubt, that a robust case can be made to demonstrate that certain information can only be acquired through the use of live animals. One example is pharmacokinetic data where the information represents the manner in which the animal absorbs, metabolises and excretes a drug over the time course of the experiment. Cell functions are easily replicated in-vitro but not organ and system functions.

Acceptability of using animals

LAVA supports the use of animals where their value as a scientific model is well justified by way of a robust cost benefit analysis and in this respect we fully endorse the principles embodied in the current UK legislation controlling the use of animals in research. We support the meaningful use of animals; a view, we believe, that is held by the majority of society who seek justification and humanitarian attitudes to the use of animals. LAVA accepts that if scientific work involving the use of animals is of real value, likely to relieve suffering, and directed towards preventing or treating disease, then, if

it is essential to use animals, that we must design experiments properly, use as few animals as possible, and waste as few as possible, and that we ensure suffering is minimised, keep the animals in good conditions, and, when they are killed, that it is done as humanely as possible. Furthermore we believe that scientists have a duty to inform public opinion on these matters but to do so effectively they deserve the support of the community so they feel able to communicate freely without fear of intimidation or reprisal from those holding opposing opinions.

LAVA is convinced of the continuing need to use of animals in order that we may advance veterinary research into improved treatments for recognised conditions or diseases and also, to address new and sometimes devastating animal diseases which emerge from time to time, e.g. feline AIDS, canine parvovirus infection etc. In these instances, we need to use the target species to develop effective treatments or preventative measures.

Suffering of an animal

The veterinary surgeon is in a unique position in being able to express an informed opinion of animal suffering and in being able to assess and advise on the relief of pain and suffering in animals. Veterinary surgeons should have empathy for animals and are trained to recognise signs of disease in animals. Furthermore, through our knowledge of comparative biology and animal behaviour, we are able to compare and evaluate the significance of various signs of pain and distress exhibited by different species. In this respect we believe we bring to the research community a particular professional perspective of what might be deemed acceptable in terms of animal suffering to achieve specific scientific objectives. For this reason, veterinary surgeons are an integral component of the local ethical review process. They provide a unique insight into the degree of suffering experienced or likely to be experienced by animals in the course of research procedures and are able to assist researchers in identifying the likely adverse effects of planned procedures and are able to advise on how those effects can be mitigated or prevented.

The experience of LAVA suggests that the degree of suffering in the vast majority of experiments is of a very low order of severity. Furthermore much of this suffering is often transient and will be reduced to the minimum by refinements in experimentation and housing.

Most project licences have a mild severity banding because the proposed interventions are not anticipated to cause pain, suffering, distress, or lasting harm to the animal.

Council must also recognise that all use of anaesthetics and analgesics in UK laboratories will be under veterinary direction whenever interventions are

anticipated to cause pain or distress to the animal, such as in procedures with moderate or substantial severity limits. The number of project licences with a substantial severity banding, of course, forms only a small percentage of the total number of licences granted.

Q2. WHAT ARE YOUR VIEWS ABOUT THE USE OF GENETICALLY MODIFIED ANIMALS IN RESEARCH?

The use of genetically modified animals has opened up many new possibilities in science. For example, use of genetic knock-out mice has allowed scientists to more accurately pinpoint disease pathogenesis, and to mimic disease models.

Scientists who work with genetically modified animals, however, should be sympathetic to public concern, should closely monitor the phenotype of the animals and seek to qualify and quantify, and thereby reduce, the severity of any alteration in animal wellbeing that arises from genetic modification. LAVA would be extremely concerned if scientists bred genetically modified animals without trying to identify any phenotypic abnormalities, unique characteristics, or particular housing needs. Furthermore we perceive significant advantages in formally documenting this information so that it may be made readily available to the scientific community. The availability of such information, presented appropriately, is also likely to go some way towards alleviating public concern. The experience of LAVA members demonstrates that many genetically modified animals are essentially the same as other animals of the species (i.e. a genetically modified mouse remains fundamentally a mouse) and in the majority of cases; there is very little physical expression of the genetic manipulation. Immunocompromised mice require appropriate housing and husbandry to remain in good health; we see this as being just as important if the immune system is compromised as a result of a spontaneous mutation than if it arises intentionally as a result of genetic manipulation. Thus, in the opinion of LAVA, genetically modified animals raise no new welfare issues unless it is known that they are likely to express some unique phenotype, a situation that can readily be anticipated and usually ameliorated provided a robust cost-benefit analysis is previously carried out.

There will also be situations where genetically modified animals can be regarded as representing an element of refinement. Where, for instance, their use might replace an older experimental model of greater severity, e.g. a surgically prepared animal.

Types of Animals that may be created

LAVA acknowledges that genetically modified animals may be perceived as being “unnatural” from the point of view that they are created, intentionally, by man using methods that would appear “artificial” to many in society. Nevertheless LAVA sees no fundamental difference in the development of this technology; neither in comparison with traditional techniques that are employed in the breeding of pedigree livestock nor in the potentially harmful outcome of GM technology compared to some of the more extraordinary phenotypes expressed in some highly inbred domestic pets or in comparison with some spontaneous mutant phenotypes.

LAVA sees no rationale for discriminating against genetic modification as a basis for creating a phenotype versus some chemical or surgical induction, in fact, as has been stated previously, in many cases the use of genetically modified animals may represent a refinement over current methods.

Other areas of research, (e.g. controversial areas or areas not discussed).

In our opinion all research animal use should be subject to an appropriately vigorous and robust cost-benefit analysis. Provided that the cost-benefit analysis is visible to society then we believe that this will assist in alleviating much public concern. In this way, research that might otherwise be regarded as more controversial simply requires greater justification to balance the perceived costs, in terms of animal suffering, against the likely benefits to society.

The use of GM animals has opened up many new possibilities in science. For example, use of genetic knock-out mice has allowed scientists to more accurately pinpoint disease pathogenesis, mimic disease models etc...

Scientists who work with GM animals should closely monitor the phenotype of the animals. That is, it would be concerning if scientists bred GM animals without trying to identify any phenotypic abnormalities, unique characteristics, housing needs etc... These should be documented and the information should be made available for the scientific community. For example, the Working group on GM animals is suggesting a “mouse passport” which is hoping to achieve this.

Best practice for creating and using GM animals should be promoted, e.g. refinements in genotyping. Again a robust cost/benefit analysis will assist the justification

GM animals raise no new welfare issues unless it is known that the neurophysiology has been altered but this can be accommodated in the cost-benefit analysis.

There is some element of refinement in GM animals as old experimental models are less severe.

Q3. WHAT IS YOUR VIEW ON THE USE OF ALTERNATIVES?

We would wish to emphasise how, as veterinary surgeons, we have a duty to try and assure good welfare and to reduce any unnecessary suffering to a minimum. We have a prime interest in promoting the use of alternatives.

There are already considerable incentives for scientists to use non-animal alternatives wherever possible, on the grounds of saving time and avoiding the bureaucracy, cost and delays to research associated with using laboratory animals.

A great deal of information is available about the current alternatives to animals through organisations such as FRAME, the Fund for the Replacement of Animals in Medical Experiments and ECVAM, the European Centre for the Validation of Alternative Methods.

Some examples of current alternatives to animal testing include:

- 1) Cell culture / tissue culture techniques - tissues derived normally from animals but sometimes from humans (including cells, tissue slices, whole organs) may be kept alive in the laboratory and used to investigate the effects of chemicals. Cell cultures are widely used in developing and screening new chemicals / drugs / vaccines.
- 2) Lower organisms - including bacteria, algae, fungi and plants. E.g. the Ames test uses *Salmonella typhimurium* to screen chemicals for their ability to damage DNA.
- 3) Vertebrates at early stages of development - chick embryos, tadpoles and rat foetuses are used in tests for identification of teratogens, and the chick embryo is used to identify possible eye and skin irritants.
- 4) Physico-chemical methods - e.g. the HPLC test has replaced mice to check the purity of batches of insulin.
- 5) Computer models - used in medicine design, prediction of biological effects, teaching, epidemiology.
- 6) Human studies - human volunteers may be used in certain circumstances where there is already sufficient evidence that a substance is unlikely to be harmful e.g. irritancy testing of certain cosmetic products.

Reference - FRAME publication - Alternatives to Animal Testing.

Much fundamental research is now carried out at cellular and subcellular level, using tissues rather than living animals. While advances are being made in reducing and refining usage of laboratory animals, LAVA considers that, in the present state of knowledge, there is no foreseeable alternative to testing new drugs and treatments for disease on living animals, because of the need to assess the response of multiple complex physiological systems in the whole organism.

We believe, however, that it is important to stress that any use of alternatives must be scientifically validated. The application of alternatives in the context of research animal use should be in line with the principles of the 3Rs; the use should represent a refinement, a means of reducing overall animal use to a minimum, and most importantly the use of alternatives, in this context, should be seen to replace the use of animals to achieve the same scientific objective. Otherwise the value of alternatives will represent little more than another means to achieve a similar scientific objective. We believe that this is a particularly important message to get across within our society in the context of the Animals (Scientific Procedures) Act where authority for the use of animals will not be granted if the purpose can be achieved, in whole or in part, by alternative methods.

It is also our belief that the scientific community needs to be appropriately educated, trained and competent in both in their use of animals and in the

application of alternative methodology. The public (indeed the medical and veterinary professions in general) should be better informed to make better judgements on the benefit derived from the considered use of research animals in comparison to the value and constraints imposed by alternative, particularly in-vitro, technologies. We suggest that a UK database of alternatives would be helpful in publicising what is available in each field of research and that the government should, quite rightly, direct appropriate resources towards fulfilling this need.

Replacements: are they scientifically valid or not. If they were, then obviously the use of animals would not be justified. If not, then animals may need to be used, but the research for alternatives should continue.

Setting of priorities

There is a need for more research into alternatives but this is on going as biology advances.

There should be a commitment to try to implement change.

Funding – all involved in the use of animals in research but government could do more as they mandate many safety tests based on animals.

More funding for looking at alternatives should be granted, e.g. the animals rights lobby should be funding this as well. Why don't they have a highly publicised grant fund for this?

Alternatives could be better used in the toxicity of medicines and chemical compounds to which man and the environment is exposed.

Sharing of information

Discriminate between basic and applied research in terms of duplication; unlikely for new entity discovery programmes to be exactly replicated but some replication required to discover new best in class compounds; some risk of duplication of safety testing due lack of regulatory harmonisation or appreciation of toxicophores. Replication to prove repeatability may be justified.

There is too much restriction placed by journals on the detail in methodology sections and too little requirement to explain refinements in experimental protocols. Much sharing of technique is conducted between peers in the research field whether they are scientists, vets or those caring directly for animals.

4. WHAT IS YOUR VIEW ABOUT ETHICAL ISSUES RELATING TO THE USE OF ANIMALS IN RESEARCH?

The moral status of animals

In our opinion animals do not share the same moral status as man. Humans possess the nature of a rational self-consciousness (understanding of justice and common morality) that helps distinguish us from animals.

Nevertheless, LAVA is also of the opinion that more research is needed so that we may more objectively evaluate how animals experience consciousness. This would assist our better understanding of welfare concerns arising from their use by society, not only in research but also across a broad spectrum of activities involving the use of animals and particularly where such use implies some deviation from their normal physiological state or removal from their natural environment.

How can we know how much animals suffer

We believe that our previous responses have addressed this issue. We believe that veterinary surgeons, by way of their training and experience, are well placed to offer sound opinion and advice on the matter. Nevertheless we are in support of further research to better understand the concept of "consciousness" in animals not only to pain but in their ability to discriminate suffering in a variety of situations where our interpretation, in anthropomorphic terms, would suggest that their well being is compromised and they would have the potential to suffer.

Justifying making animals suffer

A robust and rigorous cost-benefit analysis is essential to maximise benefits, and minimise costs.

It is morally unjustifiable to abandon the use of animals in biomedical research without scientifically valid alternatives.

The justification for making animals suffer – it is necessary to weigh up the costs against possible benefits. There can be no universally applicable rules for determining this. Cases should be treated on an individual basis.

Assess what are the benefits and costs associated with each activity care, compromise, scrutiny, and advocacy.

Environmental conditions are integral to the cost/ benefit equation

Q5. WHAT IS YOUR VIEW ABOUT THE UK REGULATIONS ON RESEARCH INVOLVING ANIMALS IN THE UK?

LAVA considers the strengths of the Animals (Scientific Procedures) Act to be:

- The system of regulation that assigns responsibilities at all levels, to all those involved in the care and use of research animals.
- The licensing system covering, respectively, the places where animals are bred or used, the scientific work for which animals are used and the people who carry out procedures on animals. Licences are granted to sites only after the Home Office Inspectorate has assessed that the facilities meet stringent minimum standards and that there is a management system in place to prevent unauthorised work. Project licences are granted only after a cost/benefit analysis has indicated that the benefits of the scientific study to man or animals are likely to outweigh the costs to the animals. Personal licences are granted only to those who have appropriate education and training and who have attended accredited training courses.
- The Act has promoted increased awareness and uptake of the Principles of Humane Experimental Technique postulated by Russell & Burch. These are the 3Rs: reduction and replacement of animals wherever possible and refinement of the procedures to which they are subjected, when there is no alternative.
- The Act has introduced formal training for all concerned with animal procedures and LAVA members play an active part in assisting in this training. Additionally through its relationship with the Royal College of Veterinary Surgeons, LAVA encourages its members to undertake postgraduate specialisation and continuing professional development.
- The requirement under the Act for each designated establishment to appoint a veterinary surgeon, to advise on all matters related to the health and welfare and provide 24 hour veterinary care to all animals used in research. This Named Veterinary Surgeon has a statutory role as advocate for the animal if it experiences any adverse effects arising from the scientific procedure. The Named Veterinary Surgeon also has the opportunity to offer advice to scientists at the planning stage of a project, both during the process of drafting a project licence application and during the subsequent phase of ethical review.
- This veterinary expertise has been beneficial to laboratory animal welfare, contributing significantly to
 - * better methods of anaesthesia
 - * better recognition of pain and the corresponding wider employment of analgesia for painful procedures
 - * the refinement of surgical procedures and post operative care of experimental animals
 - * providing enriched environments for research animals where they can socialise with other animals and express natural behaviour.

- The *Codes of Practice for Housing & Care of Animals in Designated Breeding & Supplying Establishment and of Animals used in Scientific Procedures* were initially a strength of the Act, setting out the minimum standards expected from designated establishments. Academic establishments in particular were encouraged to invest resources in making significant improvements to their animal houses. However, in LAVA's opinion, the Codes could be improved by being made less proscriptive. For example, whilst specified cage dimensions have established the minimum acceptable space for animals, LAVA believes that the Codes should also encourage best practices for care of the animals, to ensure they remain fit and healthy.
- The *Code of Practice on Humane Killing* lists acceptable humane methods by which animals on scientific procedure are killed.
- The Act has encouraged a bond between the veterinary profession and those with direct responsibility for the care of research animals, i.e. between the Named Veterinary Surgeon, the Named Animal Care & Welfare Officer and the Personal Licensee, to the benefit of animal welfare.

LAVA considers weaknesses of the Act to be:

- It is overly bureaucratic to administer. The paperwork is very burdensome and becoming more so in response to the mandatory local ethical review. This reduces the time available for Named Veterinary Surgeons to spend in animal facilities.
- It may take too long to pursue applications and amendments to project licences, causing frustration to research staff and leading to delays in carrying out scientific studies. The frustration is particularly marked in universities, where academic staff undertake fundamental developmental research for part of their time in addition to the burdens of teaching and administration. Similarly, amendments to Certificates of Designation are overly bureaucratic and time consuming to implement. Notwithstanding these comments, LAVA accepts that the Home Office is attempting to address these concerns.

LAVA considers that the framework of the Act is sound and requires no change. However, weaknesses arise from the manner in which it is implemented. The bureaucratic burden must be reduced, if scientific research in the UK is to survive and flourish in an ever-increasingly competitive global environment. Therefore a radical review of implementation needs to be undertaken, to examine how the Act might operate more efficiently.

LAVA is aware of several substantial programmes of work where sponsors have chosen not to carry out the research in the UK, because of the bureaucracy related to the Act.

There is a real danger that laboratory animal research will be removed from the UK to countries with less stringent laws and where the standards of facilities and care may be inferior to those offered here. While this scenario may appease some sections of the animal rights movement, it serves neither the interests of animal welfare nor scientific progress.

Q6. WHAT DO YOU THINK ABOUT THE INFORMATION THAT IS AVAILABLE TO THE PUBLIC ABOUT RESEARCH INVOLVING ANIMALS?

Public opinion on animal research is heavily influenced by images projected in the media and the propaganda of the animal rights movement has been very successful in swaying public opinion against animal research. In a largely urban society, many members of the public are distanced from animals and have limited appreciation of the many purposes for which animals are employed.

LAVA is concerned that the public remains ill-informed of the facts regarding animal research and the legal controls over this activity. In the MORI poll on Animals in Medicine & Science in 1999, more than half those approached agreed that "animal experiments for medical research purposes are a necessary evil". Less than one person in twenty responded correctly to a question on what percentage of medical research involves animal experimentation (5-10%); half indicated "over 50%".

While there may be scope for communicating actual statistics to the public, it is likely that the vast majority is not interested in being better informed but would appreciate reassurance that animal experimentation is necessary, is carried out humanely and is properly regulated.

There has been little opportunity to respond to the images created by the animal rights movement and present the counter argument for the continued need to use animals in research. Aggression and violence are being employed against scientists, animal care workers and veterinary surgeons at research and breeding establishments by certain anti-vivisection groups. One particular tactic has been for violent animal rights groups to target companies breeding animals for research. Workers have been targeted not only at their places of employment but also in their own homes. As a result, there is a significant risk that commercial animal breeders will transfer their operations out of the UK, with potentially devastating impact on the future of research in this country.

The law is ineffective in stopping this violence, so it is hardly surprising that scientists have tended to retreat from presenting the counter-arguments for animal research.

The Act itself was the result of many years of debate about changing public attitudes to the use of animals in research. It has resulted in enormous and significant changes in the facilities and management of laboratory animal research. Since 1986, fewer animals are being used. Studies being undertaken only after cost/benefit analysis has been carried out and emphasis has shifted significantly to maintaining animal welfare and minimising harm caused to the animals on study. Most scientists have come to regard working with animals as a privilege and not a right. Thus researchers and regulators have acted responsibly and have responded appropriately to changes in public attitude, by embracing not only the letter but also the spirit of the Act and have assumed a burden of increasing bureaucracy to ensure compliance with the legislation.

Violence and threats have recently been extended against those making financial investments in contract research establishments. Unless the violence is controlled so that scientists and animal care workers can pursue their legitimate work in peace, there can be no balanced argument presented for public debate.

LAVA is convinced of the need for more information to be made available to society so proper judgements can be made based on informed opinion. We suggest, however, that the scientific community can only be expected to contribute to the debate in an environment where they feel confident that they can speak freely with no fear of personal intimidation or reprisal. The pity is that the public are poorly informed on the use of animals and yet, in general terms, scientists have a "good story to tell". The blame for such a situation rests fairly and squarely on the shoulders of those opposed to animal experiments and successive governments who have remained tolerant of extreme measures taken by a minority in society to publicise the cause of "animal rights".

There isn't enough information about the benefits provided to research through the use of animals. The general public seems very ignorant about what exactly it involves, for instance celebrities endorse PETA and Cancer Research UK.

The government should offer more support and the animal rights lobby should be prepared to actively fund and promote alternatives. It could be highlighted how much money they receive and then how much they actually use to fund alternatives or research into them.

The risk of victimisation when scientists explain their work in a public forum severely limits full disclosure however many details of scientific methods in

submitted papers are removed by editors in the interest in brevity yet to retain their the core audience for particular journals.

Conversely are the public aware of the paucity of information relating to medicants that are regularly accepted but contain significant untested risk e.g. aspirin

In comparison what testing is required of nutraceuticals?

Every drug that requires animal testing should be highlighted and those that were discovered through using animals should be available. People appear to be naïve about what is required to get these “magical cures”.