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Royal Society for the Prevention of Cruelty to Animals (RSPCA)

We have restricted this document to brief overviews of our position and answers to the questions asked by the Nuffield Committee (which are shown in boxes), but we can elaborate on any of these issues if required. The RSPCA has commented in detail on issues such as the effectiveness of the Animals (Scientific Procedures) Act 1986 (ASPA), the cost/benefit assessment, openness, primate use, genetically modified animals and chemical testing in recent submissions to the House of Lords Select Committee on Animals in Scientific Procedures[i], the Home Office, Animal Procedures Committee and Boyd Group. We can provide any of these submissions on request.

1 The use of animals in research

The RSPCA is opposed to all experiments or procedures that cause pain, suffering, distress or lasting harm to animals. The Society's principal goal is the replacement of animal experiments with humane alternatives. Where replacement is not currently possible, the RSPCA supports and promotes the development of techniques that will result in reductions in the numbers of animals used, reductions in their suffering and improvements in their welfare.

The RSPCA's key concerns with regard to the UK regulatory system (ASPA) are that:

- Animals are sentient beings and experiments cause them to suffer; procedures causing substantial suffering are allowed under UK law.

- There is a serious conflict between the interests of humans and the interests of those individual animals used in scientific and regulatory studies; animals and their welfare are not given sufficient priority.

- Animals are individuals in their own right and their intrinsic worth is often overlooked in the drive to use them as research tools.

- The ASPA is often said to be the most stringent piece of legislation regulating animal use in the world, with Codes of Practice that set out the highest standards of housing and care. In fact, the ASPA and its Codes of Practice set out minimum guidelines, not best practice. Failure to recognise this leads to complacency and does not encourage continuous improvement.

- There is insufficient questioning of the justification for and necessity of animal experiments, both at the individual project level and with respect to research directions more broadly.

- There is inadequate implementation of the Three Rs – replacement, reduction and refinement of procedures and husbandry to reduce suffering and improve welfare.

- The RSPCA supports the concept of the Ethical Review Process as an essential factor in broadening the perspectives on the cost-benefit assessment and contributing to the implementation of the Three Rs, but is concerned at the current limited involvement of lay members.

- There is not enough innovative thinking with respect to replacing and/or avoiding animal experiments.

- Insufficient attention is paid to recognising, assessing and reducing the distress and pain caused by scientific procedures and other life events such as transport, housing, husbandry, handling and identification.

- Insufficient consideration is given to minimising negative mental states such as anxiety and boredom.

- Other concerns are illustrated within the answers to the questions set out in the consultation document.

It is the RSPCA's view that scientific 'tradition' plays far too great a role in determining the approach to a scientific question and the research methods employed. All too often the immediate response to any scientific problem is to create an animal model to try to answer it, because this is the way research in the life sciences has traditionally been done. Then, different research groups may use a variety of different 'models' to study the same problem. For example, there are several animal models used to study human HIV (*i.e.* cats/feline HIV, macaques/simian HIV, chimps/human HIV). Each is said to be a 'good model' of human AIDS but do they all represent a 'valid' approach to understanding the disease or developing a cure? Why are all three necessary; what is each model used for; do they each provide <u>useful</u> information; is there sharing of information between groups; is the knowledge from each group consolidated and applied? We consider these are critical questions to address.

Information provided by research:

i) Do you think that research involving animals provides information that is not available by any other method?

ii) Can results from research using animals be transferred to humans?

Both of these questions ask about the *generality* of research as if animal use is a single issue. It is not that simple. Animals are used for many different purposes and these two questions need to be applied specifically to each individual area of use. Absolute statements from either side of the debate about the validity of, or justification for, animal experiments deflect attention from the very real ethical dilemmas and welfare issues that exist and are not constructive in helping to resolve these.

i) If the goal is just to "provide information" then of course in many cases research on animals is likely to provide information that is not available by any other method. The important question is whether and why the information is actually required and by whom – what is its quality, value and potential application? This needs to be critically scrutinised on a case by case basis. The fact that animal experiments provide information does not make all experiments necessary, nor does the information acquired necessarily justify the infliction of suffering on animals.

ii) The validity of extrapolating from an animal model to a human must also be assessed on a case by case basis for all individual experiments. This is not just an anti-vivisectionist argument. There are mainstream scientists who question the value of animals as models in specific research areas, for example carcinogenicity tests, septic shock and anxiety.

The acceptability of using animals:

i) Does the acceptability of using animals depend upon the purpose of the research?

On a simplistic level, it may appear to be more acceptable to use animals in experiments that have a *direct* aim of reducing suffering in other animals, including humans. Thus, the public may be prepared to accept (albeit with concern and regret) the use of laboratory beagles to produce vaccines to protect their own companion dogs from disease, but are far less likely to condone using dogs to assess the toxicty of agrochemicals. However, to the individual animal that will be used and subsequently killed, the purpose makes no difference. They cannot comprehend why they are suffering and would not sacrifice their own lives and interests for others (even others of the same species). *NB* The ASPA recognises that some purposes are unacceptable whichever species is used, such as cosmetics testing or alcohol product development (see also pages 4-5).

i) Do different types of research justify the use of different animals?

All non-human animals are regarded by many, including the RSPCA, to have intrinsic worth and should never be viewed simply as means to an end. The only justification for using one animal species rather than another would be if that species would suffer less, taking into account all aspects of the research that would impact on the animal. This would include sourcing, breeding, transport, husbandry and care, experimental procedures and their effects, and the fate of the animals. Note, it is generally considered that primates suffer more in a laboratory environment because it is harder to accommodate their social and behavioural needs.

The fact that most research animals are mice and rats is frequently used to try to assuage public concerns about animal experimentation. However, when the cognitive abilities, social behaviour, housing requirements, and ability of rodents

to suffer are considered in depth, it is difficult to justify why their use should be any more acceptable than other animals.

The suffering of an animal:

i) How much do you think that animals suffer during research?

Animals undoubtedly suffer both physically and mentally during research and testing, and their suffering can be substantial. Pain, distress, fear, anxiety, social stress and boredom can be caused in many different ways including by procedures, the effects of procedures, transport, marking, inappropriate housing, handling, restraint and killing.

However, with respect to the overall level of suffering that laboratory animals experience, it is not possible for *anyone* to answer this question accurately. There are three main reasons for this; first, there is no centrally gathered information on the levels of suffering experienced by animals of different species during experiments[*]; second, recognising and assessing animal pain can be extremely difficult; third, the significant distress caused by inadequate housing is rarely considered or assessed, although this can contribute to and even exceed suffering caused by procedures.

Most of the animals used in experiments are small, 'prey' species such as rabbits and rodents, and such species are adapted to conceal signs of pathology or distress. This apparent stoicism is highly open to misinterpretation, especially by those who do not want to think that experiments cause suffering. This is exacerbated by the fact that techniques currently used to assess animal wellbeing and suffering are largely subjective[ii,iii,iv,v,vi], which in practice means that even the behaviour of those species that have a close relationship with, or are phylogenetically close to, humans (*e.g.* dogs and non-human primates) can easily be misinterpreted[vii,viii]. Empirical evaluations of behavioural and physiological indicators of animal suffering have demonstrated that subtle clinical signs of discomfort, pain or distress are often missed by human observers[2,ix,x,xi].

With respect to inappropriate housing, there is a large and increasing body of literature on the strong preferences of rodents for group housing and resources such as solid floors, refuges, nesting material and chew blocks[xii,xiii,xiv]. The consensus is that rodents are highly motivated to have these items and will suffer without them, yet these are not specified in Home Office husbandry guidelines and are frequently not supplied[xv]. Although less work has been done to evaluate the preferences and motivations of non-rodent species, 'standard' laboratory housing for all species is minimal with respect to both space and environmental complexity and it is widely recognised that this does not promote good welfare.

The common claims that most animals experience little or no suffering when used in research and testing therefore have no foundation and cannot be substantiated. It is

[*] The annual Home Office Statistics list only the number of projects licensed in each severity band. This is of very limited use, as it does not tell you how many animals were involved or what they actually experienced.

more likely that animal pain, suffering and distress is underestimated.

i)	What level of suffering do you think would be unacceptable, whatever the potential benefits of the research?

The following are examples of suffering within the current system of regulation that we consider to be unacceptable:

- Substantial suffering (as defined under ASPA) caused in any way, to any species, for any purpose is unacceptable.

- Any level of suffering (even mild as defined under ASPA) that could have been prevented is unacceptable. This includes situations where animals could have been provided with analgesia but were not, or where procedures or husbandry could have been refined but were not. For example, distress caused by restraining a primate for blood sampling would be unacceptable if he could have been trained to co-operate with the procedure. Also, in the RSPCA's view, the suffering caused by keeping primates and domestic fowl in standard caging of the size specified in the Home Office Code of Practice is unacceptable.

- Any level of suffering where the benefit is questionable is not acceptable. Examples here include:

  - where the benefit is primarily economic, such as improving agricultural traits, artificially adapting animals to inappropriate environments or cloning perfomance horses, is not justified in our view. Identifying such studies can be problematic, since researchers often claim that the benefits are also in increasing knowledge. For example, transgenic cattle with additional growth factor genes would produce more meat, but a researcher could claim that s/he was creating the animals to study the genetics of growth and development. If the researcher in question is also the main expert in the field, then it is difficult for others to judge the real benefit in terms of the purpose of the project and potential application of the results.

  - research into so-called "lifestyle" diseases such as obesity or conditions such as baldness, since the ethical acceptability of such research is a matter of debate.

  - suffering associated with fundamental research to determine, for example, the energetics of singing in birds, digestion in snakes, or the mechanism of head rotation in owls. Claims that such research could lead to medical applications in the short or long term are often made in the attempt to counter potential criticism and should be subject to especially critical scrutiny.

- The use of some species causes unacceptable suffering. For example, it is impossible to cater for the behavioural, social, cognitive and physical needs of Great Apes in the laboratory and their use would be morally wrong (as recognised within the present regulatory system).

2 Genetically modified animals

What are your views about the use of genetically modified (GM) animals in research?

The RSPCA is concerned about the welfare of all animals involved in genetic modification and in other biotechnology applications such as cloning, especially since the numbers of animals involved is continuing to increase. The Society believes that the pace of scientific development outstrips meaningful ethical debate in the field of biotechnology. It is essential that policies are developed to ensure that relevant technologies are only used where there is very strong justification and that the suffering, and wastage, of all the animals involved is

Do GM animals raise new or different issues?

minimised.

There are many ethical and welfare concerns that apply to the production and use of GM animals, including:

- There are specific procedures associated with genetic modification that can be painful such as surgical embryo transfer of manipulated embryos into recipient mice.
- The phenotypic effects of genetic modification can cause suffering and are difficult to predict.
- The technology is inherently wasteful of animals' lives and large numbers are required in both the creation and maintenance of GM lines.
- GM animals are increasingly viewed by scientists as biological tools rather than sentient animals with intrinsic value and the capacity to experience pain, suffering and distress.
- Many GM animals are 'born to suffer'; since genetically modified "disease models" may well experience pain, suffering and distress.
- The demand for the production of transgenic animals seems set to increase, even though the general aspiration is to reduce the numbers of animals used in research and testing.

Nuclear transfer cloning

In addition to genetic modification, nuclear transfer also raises a number of other issues:

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- Due to the inefficiency of the technology, a considerable number of animals are used in order to produce the cloned animals.
- A large proportion of animals produced by this technology have died shortly after birth as a result of physiological problems and other abnormalities.
- Many cloned livestock animals are overgrown at the time of birth, which can make birth difficult or necessitate caesarean section delivery.
- There is now evidence that cloned mice have a significantly reduced life-span in comparison with non-cloned controls and that all animal clones are more likely to suffer from a range of abnormalities, including tumours, liver disease, pneumonia and disorders of the immune system.
- The long-term effects of each new genetic modification and nuclear transfer cloning on animal welfare are unknown.

Are there some types of animals that should never be created? If so, what are they?

We have considered the issue of "types" of animals in three ways; as (i) species, (ii) phenotypes, and (iii) animals for particular purposes.

i) The RSPCA believes that all animals have intrinsic worth and that there are serious ethical and welfare issues with respect to the genetic modification of all species. Making a special case for some species is not straightforward and may not be justifiable, for reasons that we have outlined in section 1 of this submission. However, researchers are apparently driven to genetically modify an ever-increasing range of species, so it is important that decisions are made now regarding which species should never be modified. The RSPCA firmly believes that the genetic modification of non-human primates should not be permitted given the ethical issues raised by such developments, the large number of animals required, and the associated potential for harms.

We also believe that cats, dogs and equids should never be genetically modified. All three of these families, in addition to the order primates, currently require special justification for use under the ASPA and this should extend to a moratorium on creating GM primates, cats, dogs and equids. We understand that restrictions on the use of these animals under ASPA were established to reflect public concern rather than having an objective phylogenetic basis. Nevertheless, regulations reflect legitimate public opinion and this is a useful starting point.

ii) The creation of animals who are 'born to suffer' raises serious ethical and animal welfare issues, especially if their suffering cannot be alleviated. Phenotypes that cause substantial pain, suffering or

distress that cannot be prevented or relieved should never be deliberately created. This applies to all species and all purposes. It is vital to ensure that effective systems for animal monitoring and phenotyping are in place, in case highly deleterious phenotypes are created unintentionally (see below).

iii) There are some purposes for which the application of biotechnology is clearly not justified in the RSPCA's view, for example:

- cloning or genetically modifying animals to improve agricultural production traits;
- creating cloned or GM animals for use as companions, or for other trivial purposes, *e.g.* the glowing rabbit who was created as a "work of art";
- propagating a 'check-list' approach to the species it is possible to genetically modify and/or clone;

Some animals may be created to suffer on a long-term basis, for example from neurodegenerative diseases. Do you think this can be justified, and if so, why?

The RSPCA is concerned about the suffering experienced by animals whatever the reason for their suffering, be it the result of procedures carried out on them, the conditions in which they live, or their genetic status. The RSPCA therefore believes that it is not justifiable to create any genetically modified animal whose suffering will not, or cannot, be alleviated (as outlined above). Regardless of the real or perceived "usefulness" of such animal models, the capacity of animals to suffer, the likelihood of suffering occurring and how that suffering will be alleviated

In your view what will be the most controversial area of research involving animals in the future?

should be given greater consideration <u>before</u> they are made.

The RSPCA believes that all animal experimentation is now and will continue to be controversial. As far as biotechnology is concerned, there are several aspects that are causing the Society increasing concern:

- The 'check-list' approach to genetic manipulation and cloning involves many controversial experiments, such as the cloning of companion animals, endangered species and competition horses. These procedures are often carried out in the name of scientific progress but have, in our view, questionable scientific and ethical justification. This kind of experiment causes suffering for no good reason and undermines the intrinsic value of animals.

- The scientific quest to knock out each gene in the genome of mice is also controversial – we do not believe that it is necessary to do this, especially in cases

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where there is no human or animal disease linked to the gene, and/or no anticipated further work on the locus.

- The RSPCA believes that there is a strong risk that future research will aim to enhance agriculturally important traits, in fact this type of research is already underway in some centres. The Society is concerned that the application of this technology to farm animals may seriously compromise animal welfare, particularly as many farm animals are already at their physical or metabolic limits. Also, there is concern that transgenic livestock will be produced for ethically unjustifiable purposes – such as pigs with spinach genes created so that they become a more healthy food for humans, or animals created with decreased sentience to make them more amenable to intensive farming systems.

- Following the decision to sequence the chimpanzee genome, the RSPCA is extremely concerned that there will follow proposals to genetically modify apes and other non-human primates. As stated previously, the Society considers the genetic modification of primates to be unacceptable.

Are there other areas of research which have not been discussed here that should be considered?

There are several issues that are not addressed by the questions posed in this consultation, including:

(i) How can good welfare of genetically altered animals be ensured (including GM, mutant and cloned animals)?

It is vital to ensure that rigorous, effective welfare assessments are compulsory and that staff receive all the additional training necessary to care for and monitor GM, mutant and cloned animals. The Society has been involved in work in this area and can elaborate.

(ii) How effective is the cost-benefit assessment carried out under the ASPA when applied to projects involving genetic modification?

The effectiveness of the cost-benefit assessment of projects involving genetic modification could have been considered as part of this consultation. The cost-benefit assessment was set out at a time when few GM animals were used. Is it robust and effective enough to cope with the rapid developments in biotechnology?

The RSPCA believes that the benefits, necessity, justification and relevance of all research involving the production and use of GM animals are not scrutinised critically enough and that many animals are used simply because the technology is available. For example, the recent race to clone horses in which several research groups competed to be the first to be successful, with questionable benefit.

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(iii) Whose role is it to monitor developments in biotechnology?

There have been reports on biotechnology from a number of governmental and non-governmental bodies (*e.g.* MAFF ('The Banner Report'), APC, AEBC, and FAWC[*]). All of these have produced recommendations, many of which are similar. However, there is no system for monitoring the progress of these recommendations and many of them seem to disappear into a black hole, despite the fact that presumably those making them thought they were worthwhile. If an issue is considered sufficiently important to warrant the setting up of a working group, wide consultation and the production of recommendations, then there should be systems in place to ensure that those recommendations are progressed.

3 Alternatives

Note on the meaning of 'alternative'

It is important to be clear what is meant by the term 'alternative' in the context of animal experiments. To the general public, an alternative is likely to mean *an alternative method that does not involve using an animal.* This is the definition encompassed by section 5.5 (a) of the Animals (Scientific Procedures) Act (ASPA). However, the term alternative has, in recent years, been applied as a catch-all for any procedure that reduces the harms caused to animals in experiments, not only by replacing them (Replacement), but also by reducing the numbers used (Reduction) or causing less animal suffering (Refinement) i.e to all Three Rs. This widening of the definition is very convenient - most people using animals can say they use reduction or refinement alternatives, replacement is much more difficult.

The RSPCA welcomes and supports efforts to reduce the number of animals used in research and testing, and the refinement of procedures so as to reduce the harm to the animals used. We would emphasise, however, that the goal of the Society is the complete replacement of animals in research and testing and that the development techniques or strategies that eliminate animal use takes priority over reduction and refinement. Subsequent comments relate primarily to replacement alternatives.

Do you think that there is a need for more research into alternatives to research involving animals?

Yes. Clearly, there are scientific obstacles to developing relevant, reliable non-animal methods that can mimic the complex integrated physiological systems of humans and other animals. Therefore, there is an obvious need for scientific research to find ways of

[*] Ministry of Agriculture, Fisheries and Food (MAFF) 'Banner' report, 1995 – *'Report of the committee to consider the ethical implications of emerging technologies in the breeding of farm animals*'. Animal Procedures Committee (APC) report, 2001 – *'Report on biotechnology'*. Agriculture and Environment, Biotechnology Commission (AEBC) report, 2002 – *'Animals and biotechnology'.* Farm Animal Welfare Council (FAWC) report, 1998 – *'Report on the implications of cloning for the welfare of farmed livestock'*.

overcoming these obstacles, and developing non-animal techniques capable of addressing scientific questions about how biological systems work, how they are altered in disease, and how they are affected by chemicals and medicinal products.

This research needs to be carefully focused on specific applications of animals in testing and basic research. In some areas, such as safety testing, animal procedures are standardised and used repeatedly for the same purpose. In such circumstances, a substantial impact on animal use can be achieved by developing a replacement method that achieves the clearly defined objective of the standard animal test. Considerable effort has been devoted already to the replacement of animals in safety testing, with some success, and research in this area is likely to receive increased funding from the EU Sixth Framework Programme and from the chemical industry. The work of ECVAM is particularly important in this field, and should receive greater support from the European Commission.

Standard test methods are also used in the safety and efficacy assessment of biologicals, including vaccines, and further research efforts are required to replace the use of animals, particularly in highly distressful challenge tests. The technical problems in replacing these tests are quite different from those encountered with chemicals testing, and specific, targeted research is required for each vaccine test. Further support is needed for the work of ECVAM and the European Directorate for the Quality of Medicines (Biological Standardisation Programme) in this area.

In basic biomedical research, the objectives and designs of projects are extremely diverse and individual. In some cases, it may be possible to identify certain basic, widely used techniques that might be amenable to replacement of animals (as was the case, for example, with the replacement of the ascites method of production of monoclonal antibodies). In general, however, opportunities for replacement or avoidance of animal use in every project need to be analysed on a case-by-case basis, with due regard to the specific objectives of the research project and the scientific barriers to the use of non-animal methods. Research on alternatives should be carefully targeted at overcoming the most important and commonly encountered problems. A more consistent and concerted effort to identify suitable areas for alternatives research is needed, and a National Centre might help in this regard.

Many non-animal techniques arise from basic biomedical research, for example in the areas of molecular biology, cell culture and medical physics. These are described by the scientists concerned as ‘advanced’ rather than ‘alternative’ methods because they are developed to address scientific needs rather than to replace animal experiments. It is crucial that more research is conducted on the potential of these techniques, with modification if necessary, to replace animal use. For example, the possibility of using genomics to replace animals in toxicology has been widely discussed, but much more research on ‘toxicogenomics’ is required to develop reliable, valid non-animal methods from the available technology

Is research the most important need?

There are very important constraints on the replacement of animals in research and testing that are not of a scientific nature and that need to be addressed by means other than scientific research.

- **Tradition and conservatism**

  If researchers have always used animals themselves and are working in a field that has historically always used animals, they may be reluctant to consider a change of approach and/or see no benefit (scientific or other) in doing so. This is especially relevant in research fields such as experimental physiology, which has always depended very heavily on the use of whole, living animals and where the only alternative may be not to do the experiment. Questioning the justification for one's entire research programme is (understandably) not something that comes easily to most physiologists, who often regard the concept of alternatives as either something completely irrelevant to them or as a direct attack on their life's work. This is not easy to deal with, especially in a climate where technological advances (*e.g.* in biotelemetry) are continually pushing the boundaries of what is possible in fundamental physiology and scientists are under increasing pressure to use these techniques to the full.

  As stated on page 2 of this submission, scientific 'tradition' plays far too great a role in determining the approach to a question and the techniques that are used to try to answer it. It is vitally important that scientists consider ***alternative approaches*** to experimental goals, enabling the ***avoidance*** of animal use, in addition to striving to replace animal experiments. In many instances, the term *replacement* can actually be misleading in that it implies that an animal technique is already in place, and that the non-animal technique is brought in to replace, or displace, it. This scenario can clearly apply in toxicology, where there are established, animal methods written into testing regulations. However, even in toxicology there are instances where there is no established animal test to replace, and a non-animal test can be considered first. (An example is phototoxicity, where an *in vitro* test was accepted for regulatory purposes before an animal test was suggested).

  The RSPCA believes that there is a need for far more innovative, creative, flexible and challenging thinking in research and toxicity testing in general, on choice of method and the approach to asking and answering scientific questions. This should be encouraged at all stages of scientific education, and will necessitate a reconsideration of the way that science is taught and the way that students are taught to think.

- **Lack of incentive**

  Biomedical researchers are usually under pressure to achieve results, and solve problems, quickly. This pressure may be generated by the competitive nature of research, the need to compete for kudos and research grants and publish papers, but may also reflect a real urgency to understand and alleviate human or animal suffering. In either case, researchers will be reluctant to spend time on developing non-animal alternative methods when they believe that an available animal method will give valid results. Ways need to be found to enhance the status of work on alternatives by providing funds, time and recognition for

achievement in replacement of animals within the mainstream biomedical research community.

- **Poor communication**

  Fundamental to identifying alternative approaches is the availablity of adequate information on past and current research in specific fields. Data sharing is an important means of avoiding duplication of testing in toxicology, but greater availablity of reports of negative, or unsuccessful research, and clear presentation of the potential of new techniques would also help reduce redundancy and wastage in animal experimentation. Accessing information about suitable alternatives/alternative approaches to particular scientific questions can be difficult, partly because such information is not always published and, even when it is, is not usually indexed so as to highlight any of the Three Rs.

- Regulatory inertia

A very complex and intensely bureaucratic regulatory system has been built up to control the safety testing of products ranging from industrial chemicals to pharmaceuticals and vaccines. Many animal tests are currently required for risk assessment to support the marketing and use of these products. To replace the accepted animal tests requires considerable effort to reassure the regulatory authorities that the alternative methods provide an adequate assessment of risk, and to overcome bureaucratic inertia. Intensive efforts are needed to accelerate the validation and regulatory acceptance of alternatives through bodies such as the OECD and ICH, as well as ECVAM and the European Commission.

Who should fund research into alternatives?

The primary responsibility for funding research on alternatives lies with the users of animals for scientific purposes. The pharmaceutical and chemical industries have already invested comparatively large amounts of money in research on alternatives, largely in toxicology, and seem likely to increase that investment. The research councils, particularly the MRC, should do much more than they do, in view of the large number of animal experiments that they support. The Government also has some responsibility related to the regulatory requirements that currently demand animal testing, but it has a more fundamental obligation to act on behalf of the public, who clearly have concerns about the use of animals in science. The EU should also increase the funding of ECVAM and other organisations involved in the development and validation of alternatives.

What is most needed at present is a coordinated and carefully considered strategy for identifying priority areas, opportunities and research needs, for targeting research funds, for disseminating information, and for discussing problems and ideas. A UK centre for alternatives could achieve these objectives within the UK, but an EU centre might be more effective.

Do you have concerns about the way research involving animals is reported in scientific journals?

Yes. Life science journals rarely include sufficient information on animal use, husbandry and the Three Rs. This is a problem for the following reasons. Research publications are currently the key source of information on what actually happens to laboratory animals, so adequate detail is vital for an informed debate on the issue. The perceived benefits are always described but it is also essential to describe experimental protocols and husbandry in sufficient detail to enable adequate understanding of the impact of the research on the animals involved. This is important for animal welfare, as refinements need to be disseminated *via* papers in mainstream journals. It is also important in the promulgation of good scientific practice, as pain or distress can significantly influence results.

Despite this, it is our experience that the detail provided in many journals is minimal and does little to convey what was done to the animals or how they were housed and cared for. For example, animal housing is frequently described only as "standard" or "according to Home Office guidelines", which are minimal and open to interpretation. Where surgical procedures are described, there is often no mention of peri-operative care including pain management even when, according to the researchers involved, analgesia had actually been given.

We believe that methods sections should include more, and more meaningful, information on experimental animals and their use. It is commonly believed that this level of detail is inappropriate in refereed journals, yet such information can easily be summarised and it is the responsibility of the researcher to include and defend it.

The RSPCA is also concerned about the tendency of some research to be 'hyped' by overstating its impact or benefit, often in the hope of gaining public approval or funding. Solid organ xenotransplantation research is one example. Apart from such hype being cruel to patients who are looking to benefit from the research, this makes it impossible to carry out truly critical and accurate evaluations of whether the experimental costs, in terms of animal suffering, really are outweighed by the benefits. Certain aspects of cloning research provide further examples, where claims are made that each new successful cloning experiment will have an enormous impact on medical research, without substantiating evidence.

The reasons for cloning projects often appear ambiguous to the RSPCA. For example, a recent publication in *Nature* described the successful cloning of the horse[xvi] where the stated outcome, that the clone could be born to its nuclear donor, had actually already been reported elsewhere for goats[xvii]. That fact undermines the reported reason for publication and suggests to us that the researchers had simply wanted to see if they could clone a horse. It appears in this and other similar cases that researchers are presenting long term medical and/or scientific goals to the public in order to deflect criticism and make their animal use sound more acceptable[*].

The Royal Society is currently investigating the way in which scientific results are reported, and the RSPCA has made a detailed submission of our views on this subject to the Royal Society's call for submissions.

[*] When the existence of Prometea, the first cloned horse, was announced, one of the researchers involved initially said to the media that it would be "fun" to recreate past champions and race them against one another. Following criticism on ethical and welfare grounds, he shifted emphasis to the alleged medical benefits.

4 Ethical issues

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

The moral status of animals:

- What moral status do you believe animals have?
- Do you think there are distinctions between the moral status of different animals, such as mosquitoes, mice and monkeys?
- What differences between humans and animals could justify the suffering of animals in research that would benefit humans?

These questions are extremely difficult to answer and would require a comprehensive consultation process in themselves. However, we would make one major point with respect to differences between humans and other animals. When carefully and fairly considered, perceived differences between humans and other animals in cognitive ability, sentience, and ability to experience positive and negative emotional states, can be seen to be differences in degree but not in kind. Whatever debate there may be about moral status, it is a fact that non-human animals are used in research and testing because humans can do this and because they want to benefit from the results, even if this is solely by acquiring knowledge that interests them. The key issues for the RSPCA are the suffering and the devaluing of animal life caused by animal experimentation. We also refer the Committee to the Institute of Medical Ethics publication *Lives in the Balance*[xviii], and Boyd Group papers 2 and 3[xix] on the moral status of non-human primates. These publications have already considered some of the Nuffield Committee's questions and use an approach that we support.

How can we know how much animals suffer?

There is a large and increasing body of literature on this issue, for which we can supply references but which we will not repeat here. We also support the evidence review submitted to the Committee by David Morton.

Can we reliably extend concepts such as 'pain', 'suffering', 'distress' and 'happiness' from humans to animals?

Yes. The RSPCA takes the view that emotional states such as these are adaptive and have evolved to increase the fitness of individuals by motivating them to avoid danger, minimise damage and seek physical and social environments that maximise survival and wellbeing. We do not believe that distress in, say, a mouse is identical to distress in a human, but we do believe that the mouse's distress is real, important and an aversive experience for the individual. A further compelling reason for giving animals the benefit of the doubt with respect to emotional states is the fact that animals, including rodents, are

used in the research and development of treatments for pain, anxiety and depression in humans.

How can we assess the suffering of an animal during research?

Again, the literature and available resources on the assessment of animal suffering are increasing. See also David Morton's review and our answer to question 1, pages 3-5. There is a pressing need for better training in animal monitoring, including an understanding of animal behaviour, the potential for animals to conceal clinical signs and how to use and tailor different assessment techniques to particular studies. The report of an RSPCA survey into recognising suffering in the UK elaborates on this[3].

Should more research be undertaken to investigate how animals experience the world? If this research had to be invasive, do you still think it is important?

This is a very important question. Considering the first part, the RSPCA Science Group continually monitors the literature on animal cognition, behaviour and welfare and finds it invaluable for informing and implementing Society policy. However the Society obviously does not support research that causes animals pain, suffering, distress or lasting harm. Using the results of such research to further the cause of animal welfare presents the RSPCA with a dilemma similar in nature to that faced when using and advocating veterinary pharmaceuticals or "prescription diets".

In many cases it is possible to conduct behaviour, cognition and welfare research that is not invasive and can still be used effectively to improve the lot of animals. Where invasive studies are proposed, the ethical review should critically question their necessity and application. If there is already sufficient evidence to give animals the benefit of the doubt in a particular area, or if it appears that the study is actually curiosity-driven fundamental research rather than applied welfare research, it should not, in our view, be licensed.

5 The regulations

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

The RSPCA's key concerns about the ASPA are listed in the introduction to this submission (pages 1-2) and set out comprehensively in the Society's submission to the House of Lords Select Committee on Scientific Procedures[1]. We have set out brief answers to the specific points made by the Nuffield Committee below.

Welfare of animals:

In your view, do you think current provisions for the assessment of welfare of animals are appropriate?

No; the RSPCA believes that far more comprehensive guidance is required from those expert in the field including the Home Office, for reasons that we have set out above (see also David Morton's evidence review and the RSPCA pain survey report[3]).

When do you think welfare assessments should be conducted: before, during and/or after a project?

We assume that this refers to assessing the welfare of individual animals used in research projects, in which case the answer is all three. It is essential to obtain baseline data, before procedures begin, on all of the chosen parameters that will be monitored throughout the experimental protocol. It is also obviously vital to monitor animals as regularly and frequently as is necessary throughout the duration of the project. Following studies, animals who are not euthanased might be reused, rehomed or released; welfare assessments should therefore continue to ensure that they are not suffering or likely to suffer because they have been used in experiments (this is also a legal requirement). All of these assessments should be used to inform future judgements on probable harms caused by procedures and taken into account in future cost-benefit assessments.

Can welfare assessments for different animals be adequately captured in regulations?

It would be impractical to set out specific details of welfare assessments in primary legislation, as they will be different for each species, strain and procedure and will develop as understanding of animal welfare develops. The regulations ought to define minimum requirements for assessment, while the accompanying Home Office Guidance Notes to the ASPA should be expanded to promote and encourage appropriately comprehensive welfare assessment by providing practical examples and resources.

There are a number of other very important factors associated with welfare assessment including training in the different techniques and how and why they are used, creating and maintaining an effective and empathetic assessment 'team' and ensuring that sufficient resources are available to implement successful monitoring. These issues are covered in more detail in the RSPCA pain survey report[3].

Regulation of GM animals:

Should licences be required for the breeding of all GM animals?

Currently, all GM animals that are bred must be registered as scientific procedures and hence a Home Office licence is always required. Although some people suggest that this is inappropriate because most GM animals suffer no ill effects as a result of their modification(s), the RSPCA strongly believes that GM animals should continue to be recorded. Huge numbers of animals are involved in the breeding and maintenance of GM lines and this fact should not be hidden by their removal from the Home Office Statistics. However, GM animals may be better recorded in another way, rather than as procedures as this may distort the statistics representing animal suffering.

Another relevant issue is whether it should be possible to remove a particular GM animal or line of GM animals from the "protection" of the ASPA if the modification is shown to have no harmful effects. A licence would then no longer be required to breed the animal(s). In principle it would seem that if a GM animal is not affected by the genetic modification then there is no reason to keep them within the ASPA. However, the problems with this include the possibility that although the modification may not have deleterious effects in the standard laboratory environment, once the animal is exposed to new and potentially more challenging environments the modification may cause suffering. In addition, breeding the GM animal with different animals than have been used in the laboratory may also bring to light negative effects.

Are current regulations appropriate for assessing the welfare of a new breed of GM animal?

No; currently there are no specific regulations governing how welfare assessments of GM lines ought to be carried out. The fact that genetic modification always has the potential to impact on animal welfare means that proper assessment of each new line is essential. There is widespread recognition in the scientific community that specific welfare assessments are necessary at several time-points in the generation and maintenance of a new GM line and a CBPAR working group (with RSPCA representation) is currently investigating what should be included and when they should be carried out.

Cost-benefit analysis:

Do you consider the current provisions to be appropriate?

The need to carry out a cost/benefit assessment is in our view an essential requirement of the ASPA. However, its effectiveness in practice depends critically on a number of factors including how the costs (*i.e.* harms to animals) are defined and described, how realistically the potential benefits are presented and who is making the judgement. The concept of need, whether applied to animal experiments or anything else in life, is problematical. 'Necessity' means different things to different people, depending on the pressures that they are subjected to. Thus the crucial decision regarding whether a benefit is sufficiently desirable and necessary to justify animal suffering and/or loss of life (or expenditure of scarce resources for that matter) is clearly dependent upon the individual opinions and beliefs of those charged with making such decisions.

Setting aside the harm/benefit assessment required by the ASPA for individual projects, the process of research funding illustrates how widely views can differ. There are far more grants applied for than there is money available. Each and every applicant would argue that their research (and therefore their use of animals where applicable) is essential, necessary and justified by their own criteria. The funding sources may operate by different criteria and turn a project down since they are operating under different pressures and constraints. These may include, for example, the economic climate, shifts in research directions that make some approaches 'unfashionable', the personal prejudices or preferences of referees, and the level of competition within specific research fields.

Decisions on broader, more general issues, for example about which particular health problems to study, which research directions to pursue, and/or where to put public money are outwith the ASPA. It would no doubt be argued that the scientific peer review process contributes to these decisions and ensures that only essential research of high quality is funded. However, as stated above, most people, even within the scientific community, will differ in their views and have areas of research that they support and others (always other peoples', never their own) where they consider the potential benefits unjustified. In addition, some sectors of the scientific community seem to consider that scientists should have complete 'academic freedom' to pursue whatever scientific direction they wish. That is, without the need to prove the value of the knowledge obtained to anyone outside their circumscribed field of research or outline how that knowledge will be used – *i.e.* without considering whether it really is in the public or national interest. These views may well be applied within the peer review process.

Thus, the harm/benefit balance is inevitably going to involve subjective judgements. (It is important to bear in mind that assigning 'values' to costs and benefits may be helpful in some cases, but may only give the *appearance* of objectivity). The phrase 'cost-benefit' is

in many ways not helpful, since it perpetuates a myth that there can be a quantitative approach to the weighing, such that it can be said that the benefits 'outweigh' the costs. Yet, how can such disparate units as animal suffering and possible (usually indirect) benefits to humans, animals, science, and industry be weighed? The Chairman of the Boyd Group, Kenneth Boyd, has expressed the view that the weighing is not about trying to show that one side of the balance 'outweighs' the other, but is about trying to reduce a 'moral tension' between a desire to achieve the benefits, and regret at the harms that are caused. This sort of weighing is more like that of a judge weighing the issues in the scales of justice and is probably more appropriate.

Confidence in any harm/benefit judgement depends on: a) the approach of those who make it; b) trusting that all the relevant factors necessary to the decision will be made explicit and be rigorously considered; and c) wide consultation, in order to consider as many different perspectives on the issues as possible. Thus, whatever scheme or method for assessment and weighing is used, the quality of the final decision depends largely on the processes by which it is made - in particular, who is involved and, probably most important of all, how sensitive to the issues they are. This depends on having a variety of inputs from differing perspectives and on ensuring that everyone is adequately trained to identify and be sensitive to the issues involved. The input of the ERP with its opportunity for broad membership is very important in this respect. The RSPCA supports the development of ERPs and believes there should be greater involvement of lay participants.

At what stages in a procedure should the analysis be undertaken?

The then Chief Inspector, now Head of Animals (Scientific Procedures) Division, Dr Richmond, states that the cost/benefit assessment is a process not a one-off event at the start of a project. We agree.

It is essential to assess the costs and benefits and weigh these prior to a project being licensed. However, it is also vital to continually monitor both harms and benefits throughout a study. For example, it may become apparent that a technique causes more pain or distress than was previously thought; a refined technique may be developed; or the results of other research could devalue or negate the proposed benefit. Any of these events could change the cost-benefit balance and may mean that the project is no longer justified, in which case it should be terminated to avoid unnecessary suffering.

Retrospective review at the end of the project is also important in order to inform future judgements. It is especially important to check how effectively the harms were predicted in the licence application and subsequently detected and ameliorated, so that endpoints can be refined and more timely interventions made to prevent suffering.

'Retrospective review' is a requirement of the ERP, although this is interpreted in different ways by individual ERPs. Reviews are carried out at intervals throughout

the life of a project depending on factors such as the severity of procedures, numbers of animals and the nature of the benefit expected.

Should it be reassessed in the light of results from the research?

Yes; see answer above.

Should results be published?

See answers to question 6.

If regulation in the UK is increased further, do you think it will impede research or drive researchers abroad?

There may be a number of reasons why researchers collaborate with scientists abroad but the main reasons for concern are where this is done because the regulations in the UK are considered too onerous, and/or it can be done quicker or cheaper elsewhere. This does not of course just apply to research on animals.

The RSPCA is often told that researchers and/or industry, are carrying out work abroad for the reasons above, but we have seen little evidence to support these claims. There is, however, evidence that the prime cause of delays is scientists themselves failing to plan ahead and get applications and amendments for project licences to the Home Office in good time. The RSPCA believes that this, if anything, is causing 'delays' far more than the proper regulation of a practice that rightly causes the public a great deal of concern.

Furthermore, with the complaints regarding over-regulation, bureaucracy, and delays coming from the scientific community it would be interesting to ask exactly what the chief proponents of this message expect. Do they really want to be able to start a project on a whim, without the careful consideration of experimental design, the 3Rs and costs and benefits, as required by the ASPA? This is after all intended to ensure not only that the science is humane, but also that it is worthwhile. How much deliberation on these matters would they be prepared to undertake if left to their own devices?

The possibility that research or breeding of animals will move abroad to countries with lower standards and less concern for animals, if controls are tightened and/or standards are further improved in the UK, is also raised when developing HO Codes of Practice and other guidelines. This makes it difficult to argue for continued improvements that benefit animals and lessen the impact of research on them. It is important to find out whether transfer of work abroad really is a problem, and if so, why it occurs, so that appropriate solutions can be sought. The ideal answer would be for all countries to have levels of regulation at least equivalent to the UK.

The other reason work may go abroad is if it is banned in the UK. This is why it is important to always consider the consequences of banning research unilaterally. For example there is no point in banning the raising of antibodies by the ascites method in the UK if antibodies produced by this method are then imported from Eastern Europe. Moral problems should not be just shifted around the world.

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

The RSPCA supports and promotes greater transparency, openness and honesty regarding the use of animals in research and testing, particularly with regard to meaningful descriptions of the full impact on animals of such use.

It is difficult from the information currently available in the public domain for anyone to gain a good understanding of why animals are used in research and testing or what they actually experience. Information is either too specialised (*e.g.* scientific papers), limited in detail (*e.g.* the Home Office Statistics, reports of funding bodies and companies), or biased (*e.g.* lobbying literature).

What sort of information do you feel you need in order to make judgements about the acceptability of research involving animals?

In order to make informed judgements on the necessity of and justification for animal experiments, meaningful information is necessary on all of the following:

- **The full impact of research on animals – what animals experience and how much they suffer at each stage of their lives, *e.g.* during supply, transport, housing and husbandry, during and after experimental procedures, euthanasia.**
- The measures taken to prevent and relieve animal suffering; how effective these were.
- The purposes for which animals are used, *e.g.* the types of pharmaceutical and chemical products being developed or tested; the questions being asked in fundamental research and the reasons the answers are considered necessary (*i.e.* to put the use in context).
- The reliability and relevance of data gained from animal experiments.
- How effectively the ASPA is implemented, *e.g.* how decisions are made regarding the necessity of and justification for animal use, the implementation of the Three Rs, husbandry standards, and the quality of staff training.
- The steps being taken to develop humane alternatives and avoid the use of animals.
- How overall research directions are decided and what consideration is given to the impact of future research on animals.

The response reproduced above 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 peer review process and how the priority that ethics and animal welfare are given in this.

- The content and impact of regulatory requirements for animal testing and how the regulatory process operates.

More meaningful information would also help the RSPCA to identify areas of particular concern where efforts and resources could be focused, for example by promoting increased funding and effort directed into the development of humane alternatives for procedures that cause the greatest animal suffering. It would also provide additional opportunities to disseminate best practice and knowledge.

What would be suitable methods for informing members of the public about research involving animals and ethical issues surrounding it?

There are many different media for communicating relevant information. The key points are that it must in accessible language for the target audience and honest about the potential harms to animals and perceived benefits.

All those who create the demand for animal use are in the RSPCA's view responsible for providing information about their animal use. This includes:

- bodies funding research using animals;
- scientists carrying out the experiments using animals and others working under or associated with work under the ASPA;
- companies developing, marketing and retailing products involving animal use or testing at any stage;
- regulatory bodies whose rules stipulate the requirement for data based on animal tests;
- bodies representing the scientific community;
- the Home Office and Animal Procedures Committee.

The RSPCA believes that the Home Office should radically review the content and presentation of the annual statistics since in its current form this is difficult to analyse and is neither accessible nor meaningful. The Home Office should also publish summaries, in accessible language, of the aims, procedures and animals (numbers and species) involved in each project licensed under the ASPA. We have covered this in depth in the RSPCA submission to the Home Office made in response to a request for feedback on the statistics[xx] and we welcome the recent announcement by the Home Office tasking the Animal Procedures Committee to review the statistics publication.

Which types of people or institutions would you trust, or not trust, to provide you with balanced information about research involving animals

It is unlikely that any information provided on this contentious issue would be considered by all to be totally objective and balanced, since individuals and organisations holding opposing, or just different, viewpoints will attach different levels of importance to different types of information. However, by increasing transparency at every stage of the process of using animals in experiments, the likelihood of people readily accepting ill-informed and/or strongly biased opinion will be reduced.

Currently, the members of the public do not believe that they are being provided with accurate information. For example, in a MORI poll conducted on behalf of the Coalition for Medical Progress on 'The Use of Animals in Medical Research' (released in March 2003), only 4% of those members of the public interviewed believed pharmaceutical companies would provide honest and balanced information regarding animal experiments. On the other hand, from the same poll, animal welfare groups and veterinarians are the most trusted sources for honest and balanced information about animal experimentation. The RSPCA and presumably the public are aware that information relating to how and why animals are used and how much they actually suffer is likely to alter depending upon whom is providing it.

From our own perspective, it is difficult to list specific types of organisation or individual that we would trust or distrust. Ultimately, we believe that the RSPCA provides the most balanced information on animal research and testing because we know that we strive to do so. However, it would not be fair to answer this point without acknowledging the good working relationship and level of liaison that the Research Animals Department has with many individuals working under the ASPA in various roles. Open communication about ethical or welfare concerns, as well as on good practice and new refinements, is hugely important and enables us to focus our initiatives in the most constructive and effective way.

Do you think medicines that were developed using research with animals should be labelled to inform people of this fact? If so, what level of information should be given?

Yes. This is all part of putting animal use into context and making people aware of how their wants and needs influence animal use. It is important to develop improved product labelling that explicitly states whether animals have been involved in the testing of ingredients or the finished product – which, of course, is currently inevitable in the case of pharmaceuticals for humans and other animals. The labelling should include as a minimum the species and numbers of animals involved and the level of suffering that they experienced. Internet links to access more comprehensive information, for example on pharmaceutical company web sites, could also be provided.

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