The ethics of research involving animals

NUFFIELD COUNCIL ON BIOETHICS

Summary and recommendations

I. Background and introduction

Issues raised by research[1] involving animals have aroused intense debate, particularly in the UK. Opinion about its necessity, justification and acceptability varies widely. Discussion on the subject is often portrayed as being essentially between two positions that are either 'for' or 'against' the use of animals. This is unhelpful, since the matter itself is complex, as are the many views that surround it. A very brief overview would need to include at least the following range of positions.

One group favours the use of animals in research and emphasises the scientific and medical benefits that have arisen. Supporters of this view include most medical-research charities, many patient groups, the current UK Government and most members of the scientific community using animals. They point out that the use of animals in research has made a substantial contribution to our understanding of biological processes, and that it has been responsible for many important biomedical discoveries, including the development of a great number of therapies and preventative treatments, such as antibiotics, insulin, vaccines and organ transplantation. The development of most modern medicines has also involved animals in research and testing. Proponents, noting that in the UK animal research is strictly regulated, argue on both ethical and scientific grounds, that it must continue to alleviate suffering and to advance scientific knowledge.

Others also draw on ethical and scientific arguments but come to a different conclusion, arguing for an end to animal research. Some take absolutist positions. For example, a few campaigning organisations question the scientific validity of all animal research and want an immediate end to the practice because they believe that results from biomedical experiments on animals are not transferable to humans. Others are less focused on the scientific issues, and more concerned with the fundamental ethical question of whether it is right for humans to subject sentient animals to procedures that may cause them pain and suffering, and from which they will not benefit. Emphasising that animals cannot consent to such procedures they take an absolutist ethical position, arguing for an end to all harmful research, regardless of the consequences for human, scientific and medical progress.

A range of further positions can be found in the debate, as many people may have sympathy for some assumptions, but reject others made by those taking the two positions described above. For example, not all animal research is undertaken to advance medical progress, and some people question whether all uses are equally necessary and justifiable. They may therefore have concerns, for example, about basic research, where the usefulness of the knowledge produced may not always be clear, or certain forms of toxicity testing, where animals may experience considerable suffering. Others argue that research involving animals is too often perceived as the only means of addressing specific research questions, or that insufficient effort is made in exhausting the potential of scientific methods that do not use animals.

In 2003, the Nuffield Council established a Working Party to examine the debate in more detail, and to clarify the complex ethical issues raised by research involving animals. In this Summary of the Report we present:

- a brief outline of the focus and structure of the Report;
- a consensus statement, which summarises the agreement of all members of the Working Party on a number of general issues (Box 1);
- our principal observations with regard to the scientific rationale for using animals in different

[1] In this Report, we generally use the term 'research' in a broad sense, encompassing experiments undertaken in basic and applied research, as well as for the purpose of toxicity testing. We use the term 'testing' to refer exclusively to toxicity testing.

kinds of research and testing;

- an overview of the way in which ethical issues have been considered; and
- recommendations and conclusions arising from the consensus statement, and the discussion of scientific and ethical issues.

II. The structure and focus of the Report

The focus of this Report is on ethical issues raised by research involving animals. After a more detailed introduction (Chapter 1) and a description of the past and present context of the debate (Chapter 2), we present an outline of the ethical issues in Chapter 3. This chapter does not seek to explain or defend individual or collective positions of members of the Working Party but rather aims to provide the reader with an overview of the kind of questions that are posed by animal research. Since the degree to which animals involved in research experience pain, suffering and distress is central to the debate, we explore philosophical and practical aspects of assessing these states in animals (Chapter 4). Having provided this background we then describe a range of different scientific uses of animals which includes basic research to understand how animals develop and function (Chapter 5), the use of animals for the study of human disease (Chapter 6), genetic modification of animals in the study of disease (Chapter 7), the development of medicines and vaccines by the pharmaceutical industry (Chapter 8) and toxicological testing of potentially hazardous compounds for animals, humans or the environment (Chapter 9). We consider the scope and potential of methods that seek to replace, reduce or refine animal research In Chapters 11 and 12. After an outline of the regulatory context (Chapter 13) we resume the ethical discussion in Chapter 14 and present the views of the Working Party, inviting readers to compare their own judgements in the light of the Report with that of the Working Party. Our recommendations are presented in Chapter 15.

Box 1: Consensus statement by all members of the Working Party (paragraphs 15.3–15.20)

Research involving animals and other uses of animals

It is important to consider the ethical issues raised by animal experimentation in the wider context of the other uses of animals in society, and to take into account:

- the impact on the lives and welfare of animals that different uses have;
- the broader consequences if there were a ban on using animals in specific circumstances;
- a comparison of the benefits arising from the different uses of animals; and
- the numbers of animals involved.

The involvement of animals in research cannot be justified simply by the fact that animals are used or abused in other ways. Each use requires special consideration. Members of the Working Party noted during their own discussions and in considering responses to the Consultation that views on animal research were not always consistent with views on other uses of animals. Awareness that contradictory views are often held simultaneously is an important first step in considering the ethical issues raised by animal research.

The benefits of research involving animals

Historically, animals have been used in a wide range of scientific research activities that have provided many benefits to society, particularly in relation to the advancement of scientific knowledge, human and veterinary medicine, and the safety of chemical products.

Some of these advances might have been achieved by other means, although we cannot know this. Neither can we know what a world would look like in which animal research had never been undertaken. Hypothetically, there may have been other options which could have produced acceptable levels of knowledge and healthcare. These levels might have been lower than our current standards, but perhaps if society had deemed the use of animals for research as unacceptable, there would have been acceptance of greater limitations on scientific and medical progress. Alternatively, it is conceivable that equally good or better progress might have been achieved with other methods. The Working Party agrees that speculation about whether or not acceptable standards in basic and applied research could have been achieved in the past by means other than the use of animals is less important than the question of assessing the consequences of continuing or abandoning animal experimentation now.

It is sometimes assumed that to end animal research would be to end scientific and medical progress, but such generalisation is unhelpful. The UK Government has responded to changes in the moral climate by introducing policies that have ended some types of animal research and testing in the UK. For example, the use of animals for the testing

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of cosmetic products and their ingredients, alcohol and tobacco has ceased. Similar policies are in place regarding the use of the great apes. Independent of the moral acceptability of research, the scientific costs and benefits of abandoning specific types of animal research need to be assessed on a case by case basis. On the one hand, the possibility of the emergence of new diseases may require a reassessment of whether the abandonment of specific types of research is still justified. On the other, scientific advances that could replace the use of animals in some areas may enjoin us to assess whether further policies should be introduced to terminate these uses of animals accordingly.

The validity, usefulness and relevance of specific types of animal research, for example in relation to the use of animals for the study of human diseases, needs to be ascertained in each individual case.

Desirability of a world without animal research

All research licensed in the UK under the Animal (Scientific Procedures) Act 1986 (A(SP)A) has the potential to cause pain, suffering, distress or lasting harm to the animals used. Most animals are killed at the end of experiments. A world in which the important benefits of such research could be achieved without causing pain, suffering, distress, lasting harm or death to animals involved in research must be the ultimate goal.

We have considered the different arguments advanced in favour and against continuing specific types of animal research in Chapters 3 and 14. Some believe the imperative to protect animal welfare should be overriding, whereas others believe that the moral arguments favour the continuation of research on animals. All members of the Working Party acknowledged that these viewpoints arise from moral convictions that should be given serious consideration. This approach requires open-mindedness in trying to understand the reasons and arguments of others. Genuine willingness is also required to test and, where necessary, revise one's own moral framework.

While we trust that more progress in the moral debate can be made, we are aware that, for the near future, further moral argument alone cannot provide a universal answer as to whether or not research on animals is justified. But practical advances in scientific methods can reduce areas of conflict. For this reason, the importance of the Three Rs (Refinement, Reduction and Replacement), and especially of the need to find Replacements, cannot be overstated.

The ethical importance of the Three Rs

The Working Party therefore concludes that it is crucial that the Three Rs are, and continue to be, enshrined in UK regulation on research involving animals. The principle that animals may only be used for research if there is no other way of obtaining the results anticipated from an experiment is also fundamental. Furthermore, we observe that for moral justification of animal research it is insufficient to consider only those alternatives which are practicably available at the time of assessing a licence application. The question of why alternatives are not available and what is required to make them available must also be asked. The potential of the Three Rs is far from being exhausted. The Working Party therefore agrees that there is a moral imperative to develop as a priority scientifically rigorous and validated alternative methods for those areas in which Replacements do not currently exist. It is equally important to devise mechanisms that help in the practical implementation of available validated methods.

In applying the Three Rs it is crucial to consider not only the context of the experiments themselves but also the many other factors that can affect animal welfare, including breeding, transportation, feeding, housing, and handling. The quality of these factors and especially the ability of animals to satisfy their species-specific needs can usually be improved.

Regulation

We acknowledge that the UK has the most detailed legislative framework concerning research on animals in the world. But proper attention to the welfare of animals involved in research and the accountability of scientists who conduct research on animals cannot be achieved merely by having detailed regulations. Regulation can act as an emotional screen between the researcher and an animal, possibly encouraging researchers to believe that simply to conform to regulations is to act in a moral way. It is therefore crucial to promote best practice more actively and to improve the culture of care in establishments licensed to conduct experiments on animals.

When considering the replacement of specific types of research by alternative methods, it is important to take account of the international context in which research involving animals takes place. Many chemical and pharmaceutical compounds that have been developed are being marketed in countries or regions that have different regulatory frameworks for animal research and testing. There is a range of alternatives that have been internationally accepted for safety testing. Nonetheless, many Replacements are not universally accepted, and the process of validation is lengthy. These processes need to be optimised and initiatives aimed at abandoning and replacing specific types of animal testing at national levels complemented by initiatives at the international level. This is not to say that initiatives in the UK can only be taken once there is consensus at an international level. In the past, the UK has been a leader in working towards change in international policies related to research involving animals. This leadership should be encouraged.

Duplication of experiments on animals

Scientific experiments involving animals are sometimes repeated by the same or other research groups. In considering whether the repetition of such experiments should take place, it is important to distinguish between *duplication* and *replication* of experiments:*

- Duplication of harmful animal experiments is in principle unacceptable. We use the term to describe cases where there is insufficient scientific justification for the repetition. It occurs primarily when the scientist either does not know that another has carried out the experiment or test in question, or when he does know, but is unable to attain reasonable access to the information.
- Replication refers to repetition of experiments or tests where this is necessary for sound progress in scientific

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enquiries. The scientific method demands that research findings need to be corroborated by the same and other research groups, in order to establish the validity of the results.

The Working Party acknowledges that academic competitiveness and commercial confidentiality can sometimes complicate the sharing of information. But at its best, science is an open process, and mechanisms that prevent the sharing of information need to be reviewed carefully in terms of their justification and implications for the use of animals in research.

The context of the debate

The majority of researchers who use animals consider that despite progress in the implementation of the Three Rs, animal research will remain an essential part of their work. Furthermore, certain provisions in the current regulatory framework for approval of chemical products and medicines require tests involving animals. We conclude that it is unrealistic to assume that all animal experimentation will end in the short term. It is crucial, therefore, to create a climate in which the necessity and justification for using animals is assessed and discussed fairly and with due respect for all views.

Constructive debate would be facilitated by the provision of clear information about the full implications of research involving animals in terms of the kind, numbers and species of animals used, as well as the pain, suffering and distress to which they can be subjected. It is equally important that society should be informed about the scientific, medical and other benefits of research involving animals. Information about selected aspects of research without provision of any further context can be misleading.

All members of the Working Party agree that the use of violence and intimidation against members of the research community, research institutions, their business partners, family and neighbours, or against organisations and people representing animal welfare groups, is morally wrong and politically insidious. The freedom to promote or oppose research involving animals peacefully and democratically, however, must be maintained.

* Sometimes, animals are used in repeated experiments for the purpose of education or training. However, we have not addressed the issues raised by this particular use here, see paragraph 1.18.

III. The scientific rationale for using animals in research and testing

Although the focus of this Report is on the ethical issues raised by animal research, we also need to consider scientific questions. For if it were the case that harmful animal research provided no useful knowledge or application, it would be difficult to see how it could be morally justified. Similarly, it is important to assess which potential scientific benefits might have to be forgone, if animal research or testing in general, or in particular areas, were to be reduced or abandoned, and could not be replaced adequately by scientific methods that do not involve animals. The two principal questions which this Report seeks to clarify are therefore:

- does the scientific use of animals lead to valid, useful and relevant results in specific areas?
- is it permissible for one species to cause pain, suffering and death to another to achieve aims that benefit primarily the former species?

Across and within each area of research involving animals described in Chapters 5–9 the intended and realised benefits take a wide range of forms. Three main types can be distinguished.

- *Advancing scientific knowledge*

  Some research, predominantly basic research, has no direct application and its primary purpose is to advance scientific knowledge about the way animals behave, or develop and function biologically. The study of basic physiological processes and genetic mechanisms also falls into this category (Chapter 5).

- *Using animals as models for humans to study disease mechanisms and develop interventions*

  Animals are used as models for humans to understand disease processes and to develop effective preventative and therapeutic measures such as vaccines or medicines (Chapters 6–8). Some of these interventions may also be used in, or have been developed specifically for, animals. Such research often draws on findings from basic research.

- *Animals as models in toxicity testing*

  Animals are used to test the safety of a range of compounds that are potentially hazardous for animals, humans or the environment (Chapter 9).

We begin our discussion with the assumption that whether or not research in these areas yields valid, useful and relevant results needs to be judged on a case by case basis. For practically all basic research it can be argued that data produced are valid insofar as it is conducted in a methodologically sound manner, since any such completed research project adds to the scientific body of knowledge (provided results are made reasonably available to the scientific community). The controversies about the acceptability of basic research therefore focus primarily on its usefulness and relevance, and on the ethical question of whether it is necessary and justifiable, if it causes specific degrees of pain, suffering or distress to the animals involved (paragraphs 3.53 and 14.38). The question of validity, usefulness and relevance is more complicated when animals are used as models for humans, as the question of whether reliable extrapolations can actually be made from one species to the other, needs to be addressed. Accordingly, we consider:

- the biological basis for using animals as models for human diseases (paragraphs 4.8–4.10);
- examples of research where it has been possible to make valid and useful inferences (see for example, Box 5.2, paragraphs 6.4–6.31, 7.7–7.8, Boxes 8.1, 8.2 and 8.3, paragraphs 9.5–9.7);
- examples of research where progress has been difficult (paragraphs 6.33–6.39);
- claims that the very concept of using animals as models for humans is flawed, misleading and dangerous because a small number of products such as medicines that have involved animal research and testing in their development were withdrawn from the market because of adverse reactions in people (Boxes 8.6 and 8.7).

Conclusion on the scientific validity of animal research and testing

We conclude that because of evolutionary continuities in the form of behavioural, anatomical, physiological, neurological, biochemical and pharmacological similarities between animals and humans there are sufficient grounds for the scientific hypothesis that, in specific cases, animals can be useful models to study particular aspects of biological processes in humans, and to examine the effects of therapeutic and other interventions.

In view of the examples of research considered in Chapters 5-9 we refute two commonly encountered generalisations about research involving animals that is undertaken with the aim of yielding results that are applicable to humans: (i) that all such research is directly applicable to humans or (ii) that no animal research has ever produced results that are useful and relevant to humans. Each type of research or testing has to be judged on its own merits (paragraph 10.46). We therefore agree with the conclusion made in a recent Report by the Animal Procedures Committee (APC) that the scientific validity of animal experiments is:

> 'a condition capable of being fulfilled, but has to be judged case by case and subjected to detailed critical evaluation.'[2]

IV. Ethical issues raised by animal research

We begin the exploration of ethical issues raised by animal research in Chapter 3 by considering five main types of ethical question (Box 2). For each question, we consider commonly encountered arguments to bring clarity to the debate, to identify agreement where it exists, and to understand the rationale for the remaining disagreement.

The question of moral status

The debate about research involving animals is often reduced to the question of defining the moral status (or moral importance) of humans, and animals. We identify three views (paragraph 3.20).

2 Animal Procedures Committee (2003) *Review of the cost-benefit assessment in the use of animals in research*, p26, available at: http://www.apc.gov.uk/reference/costbenefit.pdf. Accessed on: 4 April 2005.

- There is something special about humans, and all humans possess some morally vital property that all animals lack (the *clear-line view*).
- There is a hierarchy of moral importance with humans at the apex, followed by primates and then other mammalian species such as pigs, dogs, rats and mice and other vertebrates such as zebrafish, with invertebrates (for example fruit flies) and single-celled creatures arranged towards the bottom (the *moral sliding scale view*).
- There is no categorical distinction between human and non-human animals, and that they are moral equals (the *moral equality view*).

Box 2: Ethical questions raised by animal research

- Provided there are substantial benefits associated with research involving animals, why should the use of animals require special justification?
- Can any use of animals by humans be justified? Which specific issues need to be considered in the context of research?
- What role does the unavailability of alternatives play in the justification of research involving animals?
- How does the justification of animal research relate to the justification of other uses, such as food production?
- What is the appropriate role of regulation for research involving animals?

We conclude that neither consideration of the relative moral status nor reference to the evolutionary order or uses of animals in other contexts (paragraphs 3.21-3.26), settles the question of the permissibility of animal experimentation, or of any other use of animals in a helpful manner. Exclusive focus on the concept of moral status may obscure more than it illuminates (paragraph 3.24).

Morally relevant features

We suggest instead that a promising approach is to ask what *features* of humans and animals can qualify them as moral subjects, imposing constraints or limits on how they may be treated. We do not start from the assumption that there is one 'master property' or overriding criterion. Nor, for the purpose of the discussion in Chapter 3, do we assume that there are some species that should never be used for any purpose, or that the acceptability of using species depends on how closely related they are to humans in evolutionary terms. We explore the possibility that there are no less than the following five morally relevant features. At least one, or all of these, may be applicable to specific animals, albeit to differing degrees, and with subtly distinct moral consequences:

- sentience (paragraphs 3.28–3.29);
- higher cognitive capacities (paragraphs 3.30–3.36);
- the capacity to flourish (paragraphs 3.37-3.43);
- sociability (paragraphs 3.44–3.46); and
- possession of a life (paragraphs 3.47–3.49);

Ways of considering morally relevant features in different normative frameworks

We then turn to the question of deciding how, with regard to the possible or certain benefits of research, such characteristics should be taken into account in moral decision making: through weighing of factors (for example, the degree of suffering experienced by animals versus the value of benefits of research) or through the generation of absolute prohibitions (for example, that no research should be undertaken on animals that are capable of higher cognitive capacities, such as the chimpanzees, regardless of the benefits; paragraphs 3.51 and 3.57). A consequentialist view weighs all costs against all benefits (paragraphs 3.52–3.55). A deontological view lays down particular prohibitions (paragraphs 3.56–3.57). A hybrid view contains some prohibitions and some weighing (paragraphs 3.58–3.61). Hybrid views appear to prevail in practice, both in UK regulations and in public attitudes.

Two questions are especially important in the context of hybrid views: first, what are the absolute constraints; and secondly, how are different morally relevant factors weighed within the permitted area? To answer these questions, we will always need to consider at least five questions (paragraph 14.3):

i) what are the goals of research?

ii) what is the probability of success?

iii) which animals are to be used?

iv) what effect will there be on the animals used in the experiment?

v) are there any alternatives?

Assessing pain, suffering and distress

Since the nature of any pain, suffering or distress that an animal might experience in scientific uses is crucial to assessing the ethical implications of research involving animals, we focus in Chapter 4 on the capacity of animals to experience such states, and on philosophical and practical problems in making such assessments.

We conclude that although philosophically it is extremely difficult to determine *exactly* the subjective experiences of animals, practically it is often straightforward to make meaningful approximations. The evaluation of clinical signs, the study of animal choices, familiarity with ethological and ecological data, and consideration of physiological and neurological features are all important (paragraphs 4.18–4.28). In the spirit of critical anthropomorphism therefore, consideration of scientific evidence, especially in relation to species-specific needs of animals, can be combined fruitfully with familiarity, empathy and methodological observation (paragraph 4.7 and 4.29–4.30). Nonetheless, care needs to be taken to avoid unwarranted anthropomorphism in applying terms such as pain, suffering and distress, which we use successfully in human–human interactions, to animals (paragraph 4.60).

In practice, the welfare implications for animals involved in research and testing vary greatly. Whether or not animals experience pain suffering and distress, either as a result of experimental procedures or in the wider context through breeding, transport or housing, depends on a number of factors. These include the nature of the experiment and the likely adverse effects that it may entail, standards of handling and husbandry, and the skills and motivation of those handling the animals to implement Refinements, such as in the use of pain relieving medicines or the provision of enrichments. While it is therefore impossible to generalise about the way animals are affected by research, we make some observations on the kind of factors that influence animal welfare in paragraphs 4.31–4.59. This information needs to be considered in relation to the specific uses of animals in different types of research, which are described in Chapters 5–9.

Moral agency and the role of regulation

We explore the question of what it means to be a moral agent. This concept is important in deciding what it is to be a morally responsible scientist or animal technician, and also what the role of regulation should be in generating an appropriate environment (paragraphs 3.69–3.77). We contrast two views:

- that to be a moral agent is a matter of following a set of rules or principles; and
- that the requirements of moral agency cannot be formulated in terms of a precise set of principles, but rather requires cultivating a certain set of dispositions of character, usually called virtues.

We conclude that some form of regulation is necessary for good moral practice, but that it is crucial to be aware that it may not be *sufficient* (paragraph 3.77).

The views of the members of the Working Party

There is no consensus within the Working Party as to whether one of the morally relevant features is a master property, nor whether a consequentialist, a deontological or a hybrid approach is the most appropriate framework for deciding whether or not a specific, or any, type of research is acceptable. The Working Party has therefore not been able to agree on a single ethical stance. Instead, we present an outline of four possible ethical positions that can be taken, which mark positions on a *continuum*:

- *The 'anything goes' view (paragraphs 14.16–14.20)*

  If humans see value in research involving animals, then it requires no further ethical justification (no member of the Working Party takes this position).

- *The 'on balance justification' view (paragraphs 14.2–14.27)*

  In accepting research involving animals one acts with full moral justification, while accepting that every reasonable step must be taken to reduce the costs that fall on animals.

- *The 'moral dilemma' view (paragraphs 14.28–14.40)*

  Most forms of research involving animals pose moral dilemmas: however one decides to act, one acts wrongly, either by neglecting human health and welfare or by harming animals.

- *The 'abolitionist' view (paragraphs 14.41–14.52)*

  There is no moral justification for any harmful research on sentient animals that is not to their benefit. Humans experiment on animals not because it is right but because they can (the 'weakness of morality' view, as a sub-category of the abolitionist view, is considered in paragraphs 14.52).

For each position we describe (i) the justification for using animals in research, (ii) the implications for using animals in research and in other contexts, (iii) the value attributed to research and (iv) the role of the Three Rs. The reader is invited to judge whether one or other of the positions is superior to others. In presenting them, we are clear that moral frameworks are not to be acquired and maintained in a simple 'pick and choose' fashion. Rather, they require continuous scrutiny and justification (paragraph 14.10).

Furthermore, all members agree that independently of morally relevant features such as sentience, higher cognitive capacities, capability for flourishing and sociability, the acceptance of even relatively mild experiments for great benefit depends on the acceptance of two vital moral assumptions: that the life of laboratory animals such as mice does not have *absolute value*; and that *forced consequentialist sacrifice* is acceptable. (By the latter term we mean to say that one is able to justify a morally unequal distribution of costs and benefits among different beings.) There is no consensus within the Working Party as to whether these assumptions are morally acceptable. However, all members do agree with the conditional: harmful research involving animals must be morally unacceptable if animal life is seen as having absolute value, or if forced consequentialist sacrifice is always seen as wrong (paragraph 14.6).

Public policy in the context of moral disagreement

As in the case of other ethically contentious issues, such as abortion or euthanasia, any society needs to settle on a single policy for practical purposes. Steps need to be taken to reduce as far as possible existing disagreement. At the very least, if a public policy is adopted that many believe to be morally wrong, it may lead to instability, protest and, in extreme cases, civil unrest.

We consider that the concept of the Three Rs, and the type of hybrid moral position underlying the A(SP)A (some absolute constraints, some balancing) could be accepted, or at least tolerated, by all those holding reasonable views. Clearly, neither the Three Rs nor the A(SP)A command universal respect, and hence it would be wrong to claim that these approaches could be supported fully from the positions included in the spectrum set out above. For example, abolitionists will not agree to any invasive research involving sentient animals, and hence will not be able to genuinely share a consensus permitting it under certain conditions. However, they may, in principle, be able to tolerate the approach of the Three Rs and the provisions of the A(SP)A as a *compromise*, while continuing to campaign for a change in policy. Thus, although it would be wrong to suggest that there can be a *substantive consensus* (i.e. consensus on a shared view that research can be viewed as justified), it seems right to say that in view of the current situation an enlarged *procedural consensus* is achievable (i.e. consensus that certain democratic procedures are justified, such as a system of licensing and control of animal research that is deemed necessary). By fine tuning the regulations, relaxing some restrictions and introducing others, a broader group of people could give a greater endorsement to the form and content of the regulations than has been the case so far, even if no one set of regulations would be considered fully acceptable by all (paragraph 14.59).

If this approach is to count as a fair process, several conditions need to be met.

- All involved need to be able to have access to relevant information about research involving animals, such as the goals, welfare implications and alternatives to research, in order to judge whether specific types of research are justifiable in respect of their normative frameworks.
- The discussion about appropriate policies must be conducted in a fair and informed manner, which permits all reasonable participants to argue their case. The use of violence and intimidation are highly damaging to this process and are unacceptable, as they erode the necessary climate for reasoned debate.
- There must be a genuine possibility for policies to be readjusted. For this to be achieved, there must be reliable evidence about the views of members of the public so as to judge whether specific policies need to be revised (paragraph 14.63).

V. Conclusions and recommendations

Before we present the conclusions and recommendations of the Working Party, we must clarify two important points. First, members of the Working Party who believe that research using animals is, on balance, justified, as well as those members who take the view that it poses a moral dilemma, find most research which is currently undertaken to be acceptable. They are cautious of any proposals that might undermine progress in specific areas of basic and applied sciences which, they believe, depend crucially on research involving animals. Other members who, within the spectrum of possible views, are closer to the abolitionist view, are implacably opposed to the use of sentient animals for any scientific or medical purposes. They are equally cautious of any proposals that prolong or legitimise the infliction of pain and suffering on sentient animals. We emphasise that the recommendations that follow below, several of which aim to improve the conditions in which animals are used, should not be taken to imply the acquiescence of the latter group to animal experimentation. These members acknowledge that animals are currently subjected to experiments and believe that they need protection. While they continue to advocate that the recommendations should go further in specific areas, they accept them as steps in the right direction, without endorsing research involving animals in principle.

Secondly, as implied above, because of the diversity of views and beliefs held by the Working Party, it has not been possible to achieve complete agreement on all of the recommendations by all members of the group. In our discussions, however, and in discussion with the Council, it became clear that in the context of a highly polarised debate it is important to make

unambiguous recommendations in specific areas. While it is therefore not possible to attribute to all members of the group the conclusions and recommendations presented on any one issue, all members do accept the recommendations as valid contributions to the debate, clarifying further important implications of the more abstract thoughts presented in the consensus statement above. Nonetheless, on a few occasions it did not prove possible to identify positions that were acceptable to all members. In such instances we have tried to explain the areas of disagreement and we hope that these descriptions help to clarify the nature of the underlying dispute in a constructive way (paragraph 15.21).

The Context of the debate

Statistical information about the number of animals used and the suffering involved

The *Annual Statistics of Scientific Procedures on Animals*, published by the Home Office, have an important role in providing information about animal experimentation. At the same time, there is wide agreement that the data are presented in ways that are not readily accessible to lay people, and that the presentation could be improved. In particular, the Statistics have been criticised for not providing clear answers to the following questions: (i) what is the nature, level and duration of pain, suffering and distress actually experienced by animals used in the different kinds of procedures? and (ii) how many animals are used in procedures and related activities?

The terminology used to describe the severity of projects and individual protocols and procedures is not straightforward and therefore difficult for members of the public to understand. **We recommend that the annual *Statistics* should provide case studies of projects and procedures that were categorised as *unclassified, mild, moderate* or *substantial*. Case studies should also include examples of animals used over extended periods of time and should describe not only their immediate involvement in research but also the range of factors that influenced their life experiences, such as the conditions of breeding, housing and handling** (paragraph 15.29).

Information about the suffering that animals involved in procedures experience in practice is unsatisfactory. **We recommend that the Home Office should make retrospective information about the level of suffering involved during procedures publicly available. In gathering this information the Home Office should also obtain and make available, retrospectively, information about the extent to which the scientific objectives set out in applications have been achieved** (paragraph 15.28).

The current system of severity banding for project licences and the severity limits for procedures should be reviewed, particularly the use of the *moderate* category which covers a wide range of different implications for animal welfare. For the general public, the category *unclassified*, which refers to protocols and procedures involving terminally anaesthetised animals, is too vague to be informative, and should be clarified (paragraph 15.30).[3]

We realise that the system of collecting data about the numbers of animals used in research is very complex and that care needs to be taken to avoid making existing administrative processes more onerous. **Nevertheless, we think it highly desirable to present clearer information about how many animals of a particular species experience pain, suffering and distress, to what degree, and for how long. We therefore recommend that the *Statistics* be revised to provide this information, including details about the number of animals killed under A(SP)A Schedule 1** (paragraph 15.33).

[3] We note that some explanation can be found in the *Guidance notes* on the Act (Home Office (2000) *Guidance on the Operation of the Animals (Scientific Procedures) Act 1986* (London: TSO), p32, available at: http://www.archive.official-documents.co.uk/document/hoc/321/321.htm Accessed on: 4 May 2005. However, it is unlikely that members of the public will consult this document, and it is therefore important to clarify the terminology in appropriate places, for example in the *Statistics*.

Balanced information: campaigning organisations

We encourage animal protection groups and organisations representing those involved in research using animals to produce fair and balanced literature on this subject. This should include, among other things, detailed information about both the scientific benefits and the costs in terms of the implications for animal welfare. Similarly, the advantages and limitations of using alternative methods for research need to be discussed in a realistic manner (paragraph 15.40).

Violence and intimidation

The current climate in which animal research takes place has been influenced by several factors, including protests that often entail threats, harassment and violence (paragraphs 2.22–2.24). The effects of these actions have been highly disproportionate to the very small number of activists involved.

Those who promote violence and intimidation to pursue their case against animal research often attempt to justify their actions on the basis that they are liberating animals in much the same way as the Allies liberated Europe from the Nazis. They believe the democratic process is too slow, and moreover that the voting system is invalid, in that animals are disenfranchised. In the wake of their activities are others who would not themselves use violence but who are prepared to threaten it, persuading themselves that bullying is acceptable because it is aimed at people who are themselves bullying animals. If some of those engaged in the animal rights movement were able to force research abroad or prevent multinational companies from opting to conduct work in the UK, by means of militant actions, they would claim such outcomes as a victory.

We conclude that all approaches based on violence and intimidation are morally wrong: democracy is a precious achievement that allows conflict to be resolved without recourse to violence. It cannot permit exceptions where militant activities displace debate and consensus, otherwise anyone with any strongly held view would be able to prevail over the majority. The debate about research involving animals must be conducted in a reasonable and civilised manner. Aiming to force research out of the country through the use of violence and intimidation is no solution to the complex issues it raises (paragraph 15.50).

Public debates and discussions in stakeholder fora

Much can be learned from meetings which provide a forum for dialogue and allow members of the public to discuss their views with relevant experts. **We welcome provision in the Government's Science & Innovation Investment Framework 2004–2014 for a new grants scheme 'to build the capacity of citizens, the science community and policy makers to engage in the dialogue necessary to establish and maintain public confidence in making better choices about critical new areas in science and technology.'**[4] We are aware that the way the grants scheme is operated is currently being reviewed, and that Ministers may decide to allocate funding for prioritised areas. **In view of our observation about the need to improve the quality of the debate, and also the Governments discussion about research involving animals in the Science & Innovation Investment Framework programme**[5] **we recommend that funding should be provided by the Government to identify and carry out novel ways of achieving stakeholder engagement and public debate on issues raised by research involving animals. The Office of Science and Technology (OST) should liaise with the APC and the National Centre for the 3Rs (NC3Rs) to advise Ministers on areas of particular concern.**

4 See Science & Innovation Investment Framework 2004-2014, paragraph 21, available at: http://www.hm-treasury.gov.uk/media/33A/AB/spend04_sciencedoc_1_090704.pdf. Accessed on: 21 Apr 2005.

5 Science & Innovation Investment Framework 2004-2014, paragraphs 6.16-7.20, available at: http://www.hm-treasury.gov.uk/media/33A/AB/spend04_sciencedoc_1_090704.pdf. Accessed on: 21 Apr 2005.

In addition to public events, there are a number of *ad hoc* and permanent stakeholder groups that enable discussion among stakeholders. In our own debates, we realised the importance of having members who between them hold a broad spectrum of views on animal research. This approach allowed for comprehensive consideration of relevant arguments about specific areas of research. We encourage all parties to continue to take part in such fora (paragraph 15.45).

Open laboratories

In order to improve and sustain public trust, researchers in animal research facilities must find more ways to open themselves to dialogue. **We therefore recommend that those involved in animal experimentation should take a proactive stance with regard to explaining their research, the reasons for conducting it, the actual implications for the animals involved and the beneficial outcomes they intend for society.** These discussions should take the form of a two-way process, in which scientists not only inform the public about their research, but also listen to and understand concerns by members of the public (paragraph 15.52).

Research on views of the public

Accurate information about the current concerns of members of the public are important in considering whether or not policies on research involving animals are likely to be supported by the majority of the population. However, because of methodological constraints, opinion polls are often of limited use, and there is a lack of peer-reviewed research. **We therefore recommend that the Economic and Social Research Council (ESRC) and other relevant funding bodies provide funding for research to be undertaken on the knowledge, opinions and views of members of the public on animal research, and the underlying ways of reasoning.** Particular attention should be paid to the level and quality of information that participants have prior to, and while taking part in, the research, and to the ways in which provision of information affects individual responses (paragraph 15.46).

Education

Public debate would also be enhanced by educating young people about issues raised by research involving animals, presenting all sides of the argument. More balanced materials could make an important contribution to an improved understanding of the benefits and costs, to both humans and animals, of research involving animals, particularly for use in schools. **We therefore recommend that the UK Department for Education and Skills should commission an academic department of education, which does not have close links to pressure groups or to those involved in animal research, to produce suitable materials for use across the curriculum as appropriate, especially at Key Stages 2 and 3** (paragraph 15.41).

Regulation

Cost-benefit analysis and moral agency

The cost-benefit assessment is at the heart of the regulation of research on animals in the UK. There is sometimes the view that the assessment is only being carried out by the Home Office,[6] which 'tells the researchers what to do' once it has decided on whether or not a licence application fulfils the criteria of the A(SP)A and is therefore acceptable. The APC's 2003 Report *Review of cost-benefit assessment in the use of animals in research* observed that this interpretation would be simplistic, since a number of other individuals and committees are involved in assessing directly or indirectly the costs and benefits of a project. Furthermore, we

6 The Home Office Inspectorate carries out this assessment and advises the Secretary of State who takes formal responsibility for the granting of licences.

concluded that it would be wrong to perceive acting morally simply as following rules. Instead, active and continued scrutiny of the costs and benefits is required from all those involved, before, during and after research. This responsibility cannot be devolved to regulators, and, as the APC has emphasised, the system is also not intended to function in this way (paragraph 15.55). **We therefore welcome the APC's clarification and recommend that those involved in reviewing research proposals** (Fig 13.1) **at every stage prior to submission to the Home Office consider not only the scientific aspects, but also animal welfare in appropriate detail** (paragraph 15.56).

Good science and good animal welfare are closely interrelated, and it would be wrong for the scientific review process to ignore animal welfare issues. We are aware that many funding bodies recognise this fact. In addition to assessments by internal review boards, some, such as the Medical Research Council (MRC) and the Wellcome Trust, routinely invite external reviewers to comment on welfare issues and the way the Three Rs are considered in research proposals that involve the use of animals. However, **there is anecdotal evidence that this practice is not universal, and we strongly recommend that other funding bodies review their approach** (paragraph 15.56).

Information about the cost-benefit assessment

The APC's 2003 Report, *Review of cost-benefit assessment in the use of animals in research*, provides very useful information about the application of the cost-benefit assessment in practice.[7] The Report also observes that relevant information is spread across several different documents, and recommends that **'there is a need for an easy-to-use, comprehensive list of factors to be taken into account in assessing costs, benefits and scientific validity, that could guide researchers and others engaged in ethical review under the act, such as members of Ethical Review Processes (ERPs).'**[8] **We endorse this recommendation.** Since Ethical Review Processes (ERPs) should, ideally, also include lay people, it is important that this information is provided in a way that is accessible to non-experts. **Such a document would also be of use to the general public and the same information therefore should be provided in an accessible manner on the websites of the Home Office for the general public.** These materials should include specific case studies and also a summary of the *process* of how decisions are made in practice (paragraph 15.38).

Information about licensed research projects

We note that, following an announcement by the Government in 2004, the Home Office has made available the first anonymised information in the form of *Abstracts of Project Licences*[9] in January 2005. **We welcome the principle of publishing more information, and the decision to make it available in a searchable and publicly accessible database in due course.** We also note that the information provided in the first Abstracts varies in content, level of detail and style of presentation. We therefore **recommend that the current form of presentation be reconsidered, to ensure that, as far as possible, meaningful information about the following categories is provided:**

- **the goals and predicted benefits of research;**

7 The criteria for making cost-benefit assessments are discussed in Chapters 3 and 4 of the APC's Report (see especially Chapter 4, Boxes 4.4, 4.5 and 4.6); Animal Procedures Committee (2003) *Review of the cost-benefit assessment in the use of animals in research*, available at: http://www.archive.official-documents.co.uk/document/hoc/321/321.htm Accessed on: 4 May 2005.

8 Animal Procedures Committee (2003) *Review of the cost-benefit assessment in the use of animals in research*, p73, available at: http://www.archive.official-documents.co.uk/document/hoc/321/321.htm. Accessed on: 4 May 2005.

9 Home Office (2005) *Abstracts of project licences granted under the 1986 Act*, available at: http://www.homeoffice.gov.uk/docs4/abs_projectlicences0.pdf. Accessed on: 21 April 2005. The Home Office has previously released details of ten project licences under a Code of Practice which preceded the Freedom of Information Act 2000, see Box 13.4.

- **the probability of achieving these goals;**
- **the numbers and species of animals to be used, and an explanation of why they are needed at this stage in the project;**
- **what is likely to happen to the animals during the course of the project, including adverse effects from husbandry, supply, transport and procedures;**
- **what consideration has been given to the Three Rs to achieve all or part of the research objective(s), and how they have been applied;**
- **on what grounds possible alternatives have been rejected;**
- **source(s) of funding (i.e. public, private or both) (paragraph 15.35).**

Members of the Working Party were unable to agree in which form this information should be provided. While there was a range of views, the ends of the spectrum were (i) that full project licences should be made available, in which only the names of researchers, research facilities and commercially sensitive information has been removed and (ii) that the current format, in amended form, is suitable, but needs to be kept under close review, as it may conflict with safeguarding commercial and academic competitiveness and confidentiality, and the safety of researchers working with animals (paragraph 15.36).

Development and implementation of the Three Rs

Increased information about the Three Rs in journals

In order to improve knowledge about and awareness of the Three Rs **we recommend that all journals publishing results of research involving animals consider the inclusion of a category on the Three Rs in the methodology section.**[10] Many journals now also provide supplementary information for articles on websites, and further details about the implementation on Three Rs could be provided in this way (paragraph 15.58).

Coordination of efforts between funding bodies and the NC3Rs

Medical research charities and research councils fund a large amount of animal research and should be encouraged to take more responsibility for the promotion and implementation of the Three Rs. Further to recommending that external reviewers comment on the way the Three Rs have been implemented in funding proposals (paragraph 15.56), we consider that those who fund research have two additional responsibilities. **First, in order to improve a systematic application of the Three Rs, funding bodies should request that for each project that receives funding, a short summary be submitted to the NC3Rs which describes the way in which the Three Rs were implemented in the project, which obstacles were encountered and how they might be overcome in the future.** This information would be useful to the NC3Rs in promoting exchange of experience and fostering best practice. **Secondly, based on this information, and in consultation with the NC3Rs, funding bodies should encourage funding applications for Three R-related research in areas that pose challenges (paragraph 15.59).**

Enhancing the role of the ERP

The ERP has the potential to make a greater contribution to the identification, promotion and implementation of the Three Rs and could play a more proactive role in identifying best practice and

[10] In a different context, one journal has recently reviewed its policy on the provision of information about statistical methodology in published articles. Research had revealed that this information was of varying quality, and the editors therefore decided to introduce a requirement for authors to submit specific information about statistical methods used in the methodology section of each article, see Editorial (2005) Statistically significant *Nat Med* **11**.

helping to facilitate exchange of information. We acknowledge that some organisations, particularly the Laboratory Animals Science Association (LASA) and the Royal Society for the Prevention of Cruelty to Animals (RSPCA), have organised meetings for ERP members in the past to assist this process. We support this approach and **recommend that these two organisations, together with other stakeholders where appropriate, identify a systematic and sustainable strategy to ensure that the ERP contributes most effectively to developing best practice in the Three Rs** (paragraph 15.60).

Examination of new technologies for replacement potential: Chair of the Three Rs

We have described the complex interplay leading to the development of Replacements in Chapter 11. Strategic examination of new scientific technologies for Replacement potential, their adaptation for general use and transfer of the technology could help to ensure further progress. Scientists working in basic research who develop new methods for specific research questions often do not have the Refinement, Reduction or Replacement of animal experiments as their main objective and tend not to adapt or promote new methods for this purpose. Much more 'horizon scanning' is needed. The Working Party has therefore considered whether it would be useful to institute at least one Chair of the Three Rs, to undertake research on new technologies for Refinement, Reduction and Replacement potential and to encourage students to carry out research with an emphasis on alternative methods. Several issues would need to be assessed in more detail before such a proposal could be developed further. First, the relationship of the Chair to existing initiatives and organisations that seek to promote the Three Rs would need to be clarified, to avoid duplication of effort, and to ensure that funds to promote the Three Rs are spent most effectively. Secondly, the exact profile of the Chair would need to be carefully designed to assess whether it would be more appropriate to focus the review of the wide range of new technologies in different areas of research on one of the Three Rs only, for example on Replacement. We have therefore not been able to agree on whether or not a Chair would advance and contribute to increased implementation of the Three Rs. However, **we consider that, in consultation with the NC3Rs, it would be of value if the MRC, the Wellcome Trust and other major funders of research review and explore further the proposal of establishing and funding such a Chair (paragraph** 15.61).

Thorough analysis of scientific barriers to Replacements

Difficulties in relation to implementing Replacements are sometimes cited to dismiss further consideration of the concept as unfeasible, regardless of the exact objectives of a particular research project. Some of those opposed to research involving animals also claim that a far wider range of research than is commonly assumed could be replaced by alternative non-animal methods, if there was sufficient will to do so (paragraph 11.3). In order to make further progress in the development and the implementation of Replacements, and in order to address the range of associated expectations it would be desirable to undertake a thorough analysis of the scientific barriers to Replacement and how they might be overcome. This task cannot be addressed in general terms, but requires an in-depth analysis of specific projects in particular areas of research. Since the unavailability of non-animal methods plays a central role in the cost-benefit assessment carried out under the A(SP)A,[11] **we recommend that Ministers request the APC to undertake or commission such an analysis for a series of projects with a wide range of scientific objectives**. A clear exposition of obstacles, and strategies for overcoming them would, first, allow research efforts to be focused on problems that must be overcome if animals are to be replaced for a particular purpose. Secondly, such an analysis would identify publicly the scientific problems which are thought to be insurmountable (paragraph 15.62).

11 See Home Office *Animals (Scientific Procedures) Act 1986*, Section 5 (a), available at: http://www.homeoffice.gov.uk/docs/animallegislation.html. Accessed on: 11 May 2005.

Other issues

Motivating and monitoring Reduction of research involving animals

One way of motivating and monitoring reduction of animal experiments would be to set *targets*. The most radical form of target would be to aim to abandon or phase out a specific area of animal experimentation. Members of the Working Party disagree about the setting of targets. Those who favour the approach argue that without targets there tends to be drift and fatalism (paragraph 15.65). Those who have major reservations question the feasibility of the approach and assert that those accountable can be unfairly held responsible for unrealistic expectations (paragraph 15.66).

We accept that setting targets is not straightforward:

- We welcome the concept of targets as a useful and universally used means of measuring progress towards specific aims. But we also see problems in applying such a strategy to research involving animals, where, in many cases, the setting of specific quantitative (numerical) targets is felt by those using animals in research to be unhelpful. Instead, we suggest that Reduction could be encouraged and monitored by means of a more flexible approach. One way would be to consider qualitative *markers of reduction*, for example, aimed at reducing research that causes substantial suffering. **The Government's Inter-Departmental Group on the Three Rs should undertake or commission a feasibility study to identify which kinds of reduction marker could be set in particular areas of applied and/or basic research.**
- In principle, reduction markers should only be set if they can be linked to a realistic strategy for developing the necessary Replacement methods that will not compromise the amount and quality of basic and applied biomedical research and testing that would otherwise be licensed by the Home Office. Reduction markers that 'ration discovery' are not compatible with the scientific approach.
- The development of any strategy should primarily be the responsibility of legislative bodies and governments, as should the task of providing the infrastructure and some of the funding to facilitate the process, in close consultation with stakeholders from academia, industry and animal protection groups.
- In implementing reduction markers it is crucial that initiatives at the national level are complemented, although not limited by, initiatives at the international level (paragraph 15.67).

Duplication of research

Another area where there may be potential for reduction concerns the avoidance of duplication of research or testing (paragraphs 12.6 and 15.16). There is a range of views about whether or not research is duplicated frequently (paragraph 15.69). However, we have not explored in this Report the question of the extent to which duplication occurs, or the feasibility of devising mechanisms that help to avoid the duplication of research. But we are clear that, in principle, duplication of harmful research is unacceptable (paragraph 15.16) and we therefore welcome the approach underlying the UK Government's Inter-Departmental Data Sharing Concordat (paragraph 12.6). The Concordat has recently been reviewed by the Government who commented that the agreement had ensured that 'regulators promote data sharing within the scientific community', noting also that there was no evidence that duplication was 'a significant problem in the UK'.[12] The Working Party has not been able to study the review, and

12 Home Office (2005) *Ministerial Response on the Report by the Animals Procedures Committee – Review of Cost Benefit Assessment in the use of animals in research*, p10, available at: http://www.homeoffice.gov.uk/docs4/jw280305flint_banner_report_by_the_animal_procedures_committee.pdf. Accessed on: 21 April 2005.

is hence not in a position to comment on the Government's view.[13] We also note that the APC welcomed the Concordat in its 2003 Report *Review of Cost-Benefit Assessment in the Use of Animals in Research*[14] but cautioned that it is not yet clear how effective it will be in preventing duplication of animal studies. In particular, the APC was concerned about the voluntary nature of the Concordat, and considered whether more binding measures, such as legislation, will be needed to achieve the Concordat's aims. **We endorse the APC's conclusion that the operation and effectiveness of the Concordat should be monitored carefully and reports placed in the public domain.** The Concordat will be reviewed again in 2006. Depending on the outcome of the reviews,[15] Ministers should explore whether it would be useful to request the APC to undertake a systematic study addressing in more detail specific issues raised by the possible duplication of research. Such a study could complement and develop further the review of the Concordat (paragraph 15.70).

The scientific validity of animal research and the use of animals in the study of human disease

The question about the scientific validity of animal experimentation for medical purposes is often confused with questions about complex ethical issues. Separation of scientific and ethical questions is essential if greater clarity is to be achieved in the debate about animal research. At present, there is a relatively limited number of useful systematic reviews and meta-reviews that address the question of the scientific validity of animal experiments and tests. **In principle, it would therefore be desirable to undertake further systematic reviews and meta-analyses to evaluate more fully the predictability and transferability of animal models (paragraph 10.39). We recommend that the Home Office in collaboration with major funders of research such as the Wellcome Trust, the MRC, the Biotechnology and Biological Sciences Reserach Council (BBSRC), animal protection groups and industry associations such as the Association of the British Pharmaceutical Industry (ABPI) should consider ways of funding and carrying out these reviews. In devising a strategy, priorities should be identified which, in order to respond to concerns of the public, consider, among other things, the validity of research that falls in the substantial category and research that involves primates** (paragraph 15.80).

The use of genetically modified (GM) animals in basic research

Specific problems in relation to assessing welfare may be raised by relatively novel ways of producing animals, such as genetic modification or cloning. We take the view that the focus of concern, in the case of all deliberate attempts to influence the genetic basis of animals, should be on the welfare implications in terms of the likely pain, suffering or distress.

Documentation of the phenotypic outcomes of genetic modification (i.e. documentation about the way in which animals are affected) can facilitate the future monitoring and assessment of welfare implications experienced by animals produced in the context of 'forward' or 'reverse' genetics (paragraph 5.23). **A systematic approach to the description of GM phenotypes is crucial for assessing and monitoring welfare implications, and for undertaking thorough cost-benefit assessments**. For this reason, **we recommend that more efforts should be made to establish**

13 Parliamentary Under Secretary of State Caroline Flint commented in the Government's response of 28 March 2005 to the APC's Report on the cost-benefit assessment that 'the outcome of the review' would be published as an Annex to the Minutes of the Inter-Departmental Group on the Three Rs, see Home Office (2005) *Ministerial Response on the Report by the Animals Procedures Committee – Review of Cost Benefit Assessment in the use of animals in research*, p10, available at: http://www.homeoffice.gov.uk/docs4/jw280305flint_banner_report_by_the_animal_procedures_committee.pdf. Accessed on: 21 April 2005. However, the Working Party was not able to consider this document before finalising this Report.

14 Animal Procedures Committee (2003) *Review of cost-benefit assessment in the use of animals in research*, p52, available at: http://www.apc.gov.uk/reference/costbenefit.pdf. Accessed on: 4 April 2005.

15 See footnote 14.

comprehensive ontologies[16] **in the form of databases for GM animals. These databases should not be restricted to the receipt and dissemination of phenotypic information relevant to the scientific objectives of the research, but should also provide detailed description of associated implications for welfare. Established central databases such as the Mouse Genome Database (MGD) in the USA**[17] **should be used as the primary mechanism for archiving and distributing information on GM animals**. The information should be made available on freely accessible websites for the use of the scientific community and interested lay people (paragraph 15.73).

It is also important to continue to investigate and improve current methods for assessing the phenotypic and welfare status of GM animals. Any terminology and ontology for describing specific welfare implications should be integrated with the emerging phenotype ontologies. We note that current welfare-assessment systems vary with regard to the amount of information and the degree of detail being made available. **We recommend that the NC3Rs should consider this variation with a view to advising on the rationalisation and development of phenotype and welfare ontologies and their interrelationships** (paragraph 15.74).

We also recommend that scientific journals require the submission of phenotype and associated data about welfare to databases as a condition of acceptance of submitted papers. Although scientists often routinely submit information about new phenotypes to databases such as MGD, a more systematic approach would be useful in promoting the availability of information about both the phenotype and the implications for welfare, which would help avoid duplication and improve welfare management. Data should be provided according to the requirements of the standardised transgenic mouse nomenclature (paragraph 15.75).[18]

Toxicity testing

Current trends in society suggest that there is an increasing intolerance to risk, although some commentators believe we are now over-zealous in testing requirements. We described the types of procedures typically undertaken in toxicology research in Chapter 9. In view of the severity that some toxicity testing can entail, **we endorse the recommendation of the House of Lords Select Committee *Report on Animals in Scientific Procedures* (2002) that 'the government and the scientific community should engage more in a systematic and visible search for methods involving the Three Rs in toxicology. The Government should nominate one department to take the lead in this.' We recommend that the Inter-Departmental Group on the Three Rs should coordinate this work** (paragraph 15.81).

With regard to international initiatives the Working Party is concerned about the potential impact of recent European Union (EU) legislation for new and existing chemicals testing (Registration, Evaluation and Authorisation of Chemicals, REACH), which is likely to be implemented by 2006. According to some estimates, had the initial proposal been implemented, up to 12.8 million animals could have been involved for the testing of approximately 30,000 existing chemicals (Box 9.2).[19] The conclusion that the scale of testing and use of animals did not appear to justify the additional protection afforded to society has been widely supported, and discussions about the actual implementation were still in progress at the time of writing. Whatever its final form, REACH will greatly increase animal testing across the EU. While we make no detailed recommendation in

16 An 'ontology' in this context is an explicit formal specification of terms and the relationships among them, used to underpin the construction and querying of databases.

17 See Mouse Genome Informatics (MGI) available at: http://www.informatics.jax.org. Accessed on 21 April 2005.

18 See Mouse Nomenclature Home Page, available at: http://www.informatics.jax.org/mgihome//nomen/index.shtml. Accessed on 21 April 2005.

19 Institute for Environment and Health (2001) Testing requirements for proposals under the EC White Paper – Strategy for future chemicals policy; available at: http://www.le.ac.uk/ieh/webpub/webpub.html. Accessed on 21 April 2005.

this area, it is crucial that new approaches to risk assessment that implement the Three Rs most effectively should be explored, particularly by making maximum use of data sharing and using computational and *in vitro* tissue culture methods where possible (paragraph 15.82).

The international context of animal research

Many tests involving animals are conducted to provide safety or efficacy data for regulatory authorities, in compliance with national or international legislation. Thus, if various authorities require testing to be carried out using different study designs, a single chemical that is marketed in a number of countries might need to be tested several times. Harmonisation of test guidelines, so that a single study design is acceptable to regulatory authorities in many countries, is a very valuable means of reducing the use of animals in safety and efficacy testing. The International Conference on Harmonisation (ICH) has managed to improve mutual acceptance for the pharmaceutical industry, but much still needs to be done to extend this approach to other product areas (paragraph 15.84). Increased efforts must be made to standardise and harmonise testing requirements, in order to ensure that the minimum number of animals is used at the global level. **We therefore recommend that the UK through its National Coordinators at the Organisation for Economic Cooperation and Development (OECD) makes it a priority to identify areas in which harmonisation continues to be difficult and initiates steps to increase adoption of scientifically valid protocols that entail the least adverse welfare costs to the animals involved.** We also note that under the Inter-Departmental Concordat on data sharing, regulatory authorities aim to 'press for agreement on behalf of the UK Government for fullest provisions and procedures which enable data sharing when negotiating, updating and transposing relevant European Directives and when taking part in other international harmonisation processes.' **In order to support the proposed initiative by the National Coordinators at the OECD, we recommend that the UK Inter-Departmental Group on the Three Rs should produce or commission a report on cases where less severe protocols are not recognised internationally, whether for scientific or other reasons, and make suggestions for improving acceptance** (paragraph 15.86).

International guidelines also have a crucial role with regard to welfare standards of animals involved in research. There is evidence that relevant OECD guidelines do not use important concepts such as what defines a *maximum tolerated dose, severe distress, obvious pain* or a *moribund condition* consistently. Several of the existing OECD test guidelines could also be improved with regard to issues such as environmental enrichment, and conditions of housing, as, for example, some do not specify the requirement for group housing where this would be possible. All these factors can act as potential sources of avoidable suffering for the animals, and **we recommend that the OECD review and revise relevant guidelines to achieve greater consistency and to contribute to a wider application of the Three Rs in view of current knowledge (paragraph 15.87).**

UK researchers commissioning or undertaking research or testing abroad

There are a number of scientific, Three R-related and logistical reasons why researchers may collaborate with overseas scientists, outsource research work or obtain animals or animal-derived products (such as monoclonal antibodies) from other countries. This interaction can provide a useful means of disseminating good practice developed within the UK. But there is also a need to ensure that the international nature of research is not used to introduce double standards. **We note the position statement by the Wellcome Trust, which, as a general rule, we endorse:**

> 'International research supported by the Trust is expected to be carried out in the spirit of the UK legislation as well as being compliant with all local legislation and ethical review procedures.'[20]

20 The Wellcome Trust *Policy on the use of animals in medical and veterinary research*, available at: http://www.wellcome.ac.uk/doc%5Fwtd002764.html. Accessed on 21 April 2005.

Further to the requirement implied in this statement, some members of the Working Party would like to see formal provisions in place which ensure that research and testing, both nationally and internationally, is always carried out in accordance with the least-severe protocols, in order to minimise harm to animals used in research. They would also welcome the introduction of regulations that would prevent UK researchers from importing or outsourcing research or research products that it would not be possible to obtain in the UK. Other members of the group, while welcoming the aspiration behind such proposals, have reservations about their appropriateness and feasibility. Members also differ in their views as to whether UK-based research is being driven abroad because of the current, or likely future, regulatory provisions and practice. Despite these disagreements, all members of the Working Party emphasise that maintaining high standards in the UK has the potential to continue to influence regulations positively elsewhere. At the same time, the provisions of the A(SP)A and their implementation also need to be reviewed regularly in the context of national and international developments in policy and public debate (paragraphs 15.88–15.91).