British Psychological Society: Research Board's Standing Advisory Committee on the Welfare of Animals in Psychology

We welcome the Paper and discussion of the important issues raised within it, although we also recognise overlap with a number of other recent consultation exercises. In our response we have generally focused on the way in which the questions raised by the consultation paper apply to the study of brain and behaviour, since this is the relevant domain with which the British Psychological Society is concerned.

We suggest that it would have been more appropriate to have included in Section 1 (Background) the statement that appears on p.21 – namely, 'that the UK has the strictest system of regulation on research involving animals worldwide'

Q1 What is your view about the use of animals in research?

The past decade has seen a welcome increase of our ability to study brain function and behaviour in relatively non-invasive ways both in human and non-human animals. We expect continued improvement in our ability to both image brain function (e.g. *f*MRI and related techniques) and to disturb brain function briefly and irreversibly (e.g. TMS). However much important work aimed at uncovering the biological basis of behaviour still requires the use of more invasive studies in non-human animals. Such studies both advance our fundamental knowledge of the way in which the nervous system operates as well as laying the basis for treatment of common psychiatric disorders. Research involving animals frequently provides information that is not readily available by other methods. At best, much biomedical research on humans provides correlational data but even high correlations do not imply causality. Among other advantages (e.g. simplified systems), animal research allows the degree of control and precision of intervention necessary to establish cause-effect relationships. Such work not only helps to limit the range of possible explanations for certain normal and abnormal phenomena, but also leads to the development of general principles and models. That said, the results of animal research cannot and should not be automatically generalised to humans i.e. the animal-derived principles or models must be empirically confirmed using human subjects. Thus experimental studies in non-human animals remain central to advancement of our knowledge of both fundamental and applied aspects of brain and behavioural function. Specific examples would include the use of non-human animal models in the development of novel treatments in neurodegenerative disorders such as Alzheimer's and Parkinson's disease, and the use of animals models in the development of drugs treatments for schizophrenia, depression and anxiety.

The question of the extent to which studies in non-human animals are relevant to understanding of human physiology and behaviour is complex,

perhaps especially so in the area of brain and behavioural studies. The broad similarity of behaviour in vertebrate, and especially mammalian, species that was eloquently documented by Charles Darwin in the "The Expression of the Emotions in Man and Other Animals" is paralleled by the similarity in brain structure and function in different mammalian species. Thus the broad functions of specific brain areas show considerable conservation across species. However it is also the case that there are important differences between species. The eminent French physiologist, Pierre Flourens is renowned for his emphasis on the importance of method in science – the method creates the results. In this context, research projects must use the best available methodology including the optimal choice of species. This is especially obvious in relation to studies of drug action in non-human animals. For example, the neurotransmitter serotonin is known to act through multiple receptor subtypes, and a number of clinically valuable agents (from anti-migraine drugs to antidepressants) target serotonergic systems. Studies in the rat and mouse have been very useful in uncovering the broad functions of some of these receptor subtypes, such as the serotonin$_{1B/1D}$ receptor, in all mammalian species, including humans. However it turns out that there are species differences in the structure of serotonin$_{1B}$ receptors that mean that studies of particular drugs in rat and mouse are a poor predictor of their efficacy in humans. Thus, when it comes to applying the fundamental knowledge gained from studies in non-human mammals it will often be appropriate to move to in-vitro systems using cloned human receptors in order to complete the drug development process.

The extent to which use of non-human animals in research is acceptable is clearly contentious even within a body such as the British Psychological Society. However there is broad agreement that the Animals (Scientific Procedures) Act provides an appropriate framework, through the use of cost benefit analysis, in judging whether the use of non-human animals is appropriate within a particular research project. We have supported, through our participation in the Boyd Group, bans on the use of old world primates in the any intrusive research programme, the use of any protected species in cosmetic testing and a number of similar initiatives because they are unlikely to ever pass the test of such a cost-benefit analysis.

The extent to which individual animals may suffer as a consequence of particular research programmes is hard to quantify. Therefore the moral position must be to assume that all animals are capable of experiencing some level of pain and distress. Every effort must be made to minimise such distress including full attention to the basic principles of animal care and welfare. Routine monitoring of animals during an experiment (including observations in the home cage environment) will reveal such distress - through changes in behaviour, physical appearance and bodyweight - permitting appropriate action. We also strongly support the use of measures

that are likely to reduce any such suffering, from improved caging and environmental enrichment to specific modification of particular protocols, such as the improvement of analgesic measures before, during and after surgical procedures. However we also recognise that the implementation of such techniques may itself impair the value of particular experiments. Thus, the use of opiate analgesics may detract from the value of studies of the biological basis of opiate addiction. In other cases, the induction of distress is an integral component of the experiment (e.g. the study of disease), as indicated by current Home Office severity banding. The more severe the rating, the greater the estimated benefit-to-cost ratio. In view of these considerations, the issue of suffering should more appropriately considered from the viewpoint of the 'un-necessary' rather than the unacceptable. There are many human diseases/disorders that are unacceptable from the viewpoint of associated suffering, and especially so if development of a treatment or cure is precluded by sanctions against the use of valid but severe animal models.

Q2 What are your views about the use of genetically modified animals in ***research?***

GM animals (knockouts, knockins, transgenics) do raise some specific issues:

1. Gene deletion or insertion of an extra gene can radically influence normal development – to the extreme extent that the animals simply do not survive to adulthood. Less extreme are those instances where normal physical and/or behavioural development is adversely affected – as these changes are not often predictable, it is essential that even greater attention than normal is paid to basic animal care and welfare (including close observation of home cage behaviour).
2. As it is expensive to create a GM line, relatively small numbers of animals are available for testing leading to their extensive use in test batteries. This raises important questions regarding re-use of animals.
3. Some of the techniques that are involved in either creating or breeding genetically modified animals require careful consideration.

However similar issues to these are raised by studies using older selection techniques that lead to a change in the genetic characteristics of an experimental population.

Clearly certain types of genetic modification are likely to raise serious concern, to the extent that they should not be created. For example, highly aggressive or fecund GM rodents could in theory have major effects on local ecosystems. Fortunately writers such as Margaret Atwood, in her recent novel Oryx and Crake, give us the opportunity to reflect on these issues well in advance of any likely implementation!

The extent that suffering arises as a result of particular manipulations is also difficult to predict. Models of neurodegenerative disorders may result in long term abnormalities in behaviour, but it does not necessarily follow that these will involve protracted suffering.

One contentious area not specifically identified in the report concerns the use of techniques that greatly increase mutagenesis, though not in any targeted or hypothesis-driven manner. We recognise that these techniques raise particular ethical questions and suggest that the Council might wish to investigate them in more detail.

Q3 What is your view about the use of alternatives?

The introduction to this section slightly overstates the law in this area. The Act says that "…the purpose of the programme to be specified in the licence cannot be achieved satisfactorily by any other reasonably practicable method not entailing the use of protected animals…"

We strongly support the principles underlying the 3 R's and believe that they should be an important and explicit component of any research programme that uses non-human animals. However we also recognise the only form of replacement for behavioural research involves replacing non-human animals with human participants.

Research into the 3 R's should be supported by mainstream funding bodies in the area. For example, we support the prioritising of welfare related research by the Animal Sciences committee of the BBSRC. We believe that there is also an important role for funders, including animal welfare charities, with a specific interest in the area. Such bodies might have a particular role in funding a "Centre for Alternatives".

A Centre for Alternatives was proposed by the recent House of Lords enquiry, and would have a valuable role in coordinating research and disseminating best practice. In the different arena of Higher Education teaching, centres such as the LTSN Centre for Psychology have been invaluable in disseminating best practice and show that a relatively small group with good networking, web presence and the ability to commission small-scale research, can have an important impact on their area.

We also support funding that the raises the profile of such research in undergraduate teaching. For example, both the Society and UFAW support undergraduates carrying out welfare related research during the university summer vacation, and such proposals are sometimes explicitly directed at improving the welfare of laboratory animals.

Your guidance suggests that the issues surrounding unnecessary duplication of research might also be dealt with here. Although, in a worldwide context, there is undoubtedly some un-necessary duplication of animal research we need to be careful in distinguishing between duplication and replication. Replication is an essential component of research, especially when the replication is reported by an entirely independent laboratory. However, in many instances, once firmly established in the literature as a replicable phenomenon, it should be the responsibility of journal editors and referees to guard against unnecessary duplication. Researchers thus also have a vested interest, beyond any ethical principle, to avoid unneccesary replication if they wish to achieve the goal of publication. In addition, it is important to emphasise the term 'unnecessary' since some duplication is actually essential – as in the inclusion of positive control groups in experimental designs.

Q4 What is your view about ethical issues relating to the use of animals in research?

We shall not comment directly on the moral distinctions between use of non-human and human animals in research. These are important areas, but not our province, and also ones in which there would be a wide divergence of view within the Society. Although moral distinctions are sometimes made on the basis of differences in self-awareness, rationality and capacity to suffer, such distinctions are problematic - in so far as we have no definitive methodology whereby such attributes can be reliably assessed in non-human animals and compared directly with humans. Rather, in many instances, rank orders (hierarchies) appear to derive purely from evolutionary closeness to the human species (apes over monkeys over mice etc). This may or may not be a valid stance; much more research is needed on how various species experience the world.
The extent to which different animals experience pain and suffering is also hard to ascertain. However, to the extent that all animals protected under current legislation share basic aspects of brain systems that mediate response to aversive stimuli, and show disturbance of behaviour when exposed to such stimuli, we should assume that they can indeed experience such states. In humans our advanced ability to look into the future certainly contributes to the way in which we experience pain and related aversive states. It is likely that this aspect of pain is much less developed in most other non-human animals.

Generally speaking, the use of animals for medical and veterinary research must surely rank as highly as their use for food and above their use for clothing, pets and sport.

Q5 What is your view about the UK regulations on research involving

animals in the UK?

The UK regulations, and more especially the framework within which they are enforced, provide for a genuinely positive dialogue between researchers (as project license holders), ethical review committees (including lay representation), veterinary surgeons and Home Office Inspectors. Although there is sometimes concern about delays that arise at some points, the overall system has produced a very welcome increase in the weighting and concern given to ethical and welfare issues raised by this type of research. The presumption that welfare assessment and cost benefit analysis are processes that continue through the life of any research programme is very helpful in this regard.

Current provisions for the assessment of animal welfare might benefit from a more informed approach to behavioural (as opposed to physical) assessment. Such assessments should certainly be conducted both before (i.e. as baseline) and during an experiment. Whether assessment is necessary after an experiment depends on the nature of that experiment; usually, animals are killed at the end of a study unless authority has been granted for re-use. In the latter circumstances, it would be imperative to conduct a post-experiment welfare assessment. Welfare assessments for different species could be adequately captured in the regulations through reference to 'species appropriate' or 'appropriate for the species concerned' – this would require at minimum cross-reference to a database covering all species used in laboratory research. Licence applications should include full detail on the nature and timing of any and all welfare assessments.

Licences should be required for the breeding of all GM animals, and the granting of such licenses should carry the legal obligation for the breeder to conduct comprehensive developmental and welfare analyses on all GM lines, and to report the results to the HO. We see no alternative to the initial use of welfare assessment protocols currently used with non-GM animals; however, feedback from their application to GM animals should lead to appropriate refinement. At present the annual statistics issued by the Home Office conflate the numbers of mice used in creating and maintaining GM lines and those actually used in experiments. This seems problematic since the resultant figures seriously misrepresent (overestimate) actual experimental use.

For reasons already outlined, the current provisions regarding cost-benefit analysis are appropriate but should perhaps be informed by expert opinion on the probability of success. Not only should cost-benefit analysis be undertaken in advance of the experiment (i.e. at the project application stage), it should be an ongoing process through to completion. The argument here is that the researcher must be continually sensitive and responsive to

observed variations in factors relevant to *both* sides of the equation. Project license holders would be obliged to immediately communicate any negative deviations from the initial cost benefit analysis (along with proposed actions) to the local Ethical Review Committee and the Home Office.

Notwithstanding these points, should the impact of regulation in the UK be further increased, research will most definitely be impeded and, as a direct result, internationally ranked researchers will be driven abroad. Frustrations with present regulations and delays in the processing of licence applications may have already contributed to a significant brain drain.

Q6 What do you think about the information that is available to the public about research involving animals?

At least in relation to scientific research, the pressure for all parties is for full public access to the results of research. Researchers wish to ensure such access so that the results of their research contribute to the purposes for which it was undertaken. They will be especially keen to see that the research is published, and the only limitations on full access are likely to come from copyright restrictions imposed by journal publishers.

Explicit labelling for products developed using research on animals would at the very least help to better inform the general public that virtually every useful medicine has been developed in this manner. At present, this message is only implicitly conveyed through the very few products labelled as not having been tested on animals.