Submission by the RSPCA to the Academy of Medical Sciences/Medical Research Council/Royal Society/WellcomeTrust study on the use of non-human primates in biological and medical research.

1. Introduction

1.1 RSPCA policy on the use of non-human primates

The RSPCA, as a matter of policy, is opposed to all experiments that cause pain, suffering or distress to animals. The use of non-human primates (hereinafter referred to as primates) in scientific research and testing is a matter of particular concern because of the highly developed cognitive abilities of these animals, and the inherent difficulty in fulfilling their complex social and behavioural needs in a laboratory environment. The Society therefore believes that experiments on primates should be replaced with humane alternatives as a matter of utmost urgency. The RSPCA further believes that great apes should never be used in research that involves invasive procedures and/or confinement in a laboratory environment - the current ban on the use of these animals in the UK should be translated into law, and there should be a ban on their use world-wide.

The RSPCA is the largest animal welfare organisation in the UK with a dedicated membership of over 70,000 and an additional much larger supporter base. The Society operates throughout Europe through Eurogroup for Animal Welfare, and supports major animal welfare organisations in many other countries through its international programmes. Serious concern about the use of primates in research is evident in all the countries within which the RSPCA works and/or has contacts. The Society's policy and strategy with respect to primate use therefore reflect a sizeable proportion of public opinion.

1.2 Context of this submission

This submission has been prepared by staff in the Research Animals Department (RAD) of the RSPCA who are all qualified to MSc/PhD level in biological sciences. Their relevant expertise includes: legal and ethical issues relating to the use of animals in the biomedical sciences, cost/benefit assessment under the Animals (Scientific Procedures) Act 1986 (ASPA), education and training, animal behaviour, pain recognition and assessment, physiology, virology, transgenic technology, regulatory toxicology and *in vitro* alternatives to animal experiments. RAD staff regularly visit research establishments, are members of local Ethical Review Processes (ERPs), initiate and participate in UK and EU working groups on a wide range of issues relating to the regulation, care and use of animals, and the regulatory requirements for such use. The Head of RAD, Dr Maggy Jennings, is a member of the APC Primates Sub-Committee, the Nuffield Council Working Group on the Ethics of Animal Experiments, the board of the National Centre for the 3Rs and the Boyd Group and is therefore fully aware of the initiatives that all of these groups (mentioned in the terms of reference) are engaged in, and of the extent and limitations of these.

2. Response to the terms of reference

RSPCA staff have a broad knowledge of the research fields where primates are used and review project licence applications involving primates as part of their work within ERPs, the Animal Procedures Committee (APC), and on ethical review panels within the European Commission. However, we are not expert in these research areas, or in

alternatives other than within regulatory toxicology. We have therefore focussed on the ethical and animal welfare issues, but have also set out a number of principles that we believe are important with respect both to the scientific basis for using primates, and to their replacement with alternatives.

2.1 Scientific basis for primate use (terms of reference point 1)

We welcome the statement that the analysis of the scientific need for primate use will not be performed in isolation from ethical issues, since even if a piece of research is proven to be 'valid' and have 'benefit', it may still be deemed unjustified for a variety of reasons.

2.1.1 Scientific basis for using primates

In most fields of research where primates are used, the scientific justification given for using these animals is their close similarity to humans which it is argued makes them 'the best model'. However, researchers using other species also argue that the animals they use are good models, and different research groups may use a variety of different 'models' to study the same problem. For example, in AIDS research there are several species said to be a 'good model' for studying human HIV (i.e. chimpanzees/HIV, macaques/SIV, cats/FIV, and SCID and transgenic mice/HIV). Why are all these necessary? What is each model used for? Do they all represent a 'valid' approach to understanding the disease or developing a cure? Do they each provide *useful and clinically relevant* information? What would be the real consequence if some of this work were not done? Is there adequate sharing of information between groups? Is the knowledge from each group consolidated and applied? How far is the development of a new model in itself a scientific goal? We are not convinced that these questions are adequately considered, and we would hope the Working Group will be examining these points *in detail* for every area of primate use, rather than accepting that this is an inevitable consequence of the similarity of human and non-human primates.

We also ask the Working Group to consider whether there is a sufficiently well thought out strategy for dealing with particular human diseases or pathologies which takes account of, and minimises, animal use. Experiments on primates can deliver knowledge but at a considerable price for the animals, and this may not be the only or best approach to a human health problem. The RSPCA is frequently told that industry and funding bodies would not fund research that was not scientifically valid and necessary, that scientific peer review ensures that this is the case, and that the scientists engaged in research are able to judge the validity and necessity of their work because of their expertise in the field. However, all of these individuals and groups are likely to have a mind-set predetermined by their experience of research carried out on specific animal models. Those involved directly with a proposed research programme, whether as funders, regulators, or the scientists themselves, may be too close to (and dependent upon) the research, or have too much of a vested interest, such that they are neither willing nor able to challenge the 'traditional' animal model approach.

We ask the Working Group to explore how often peer review panels of research funding bodies sit back and really think creatively about whether there is an alternative approach to a scientific problem (note this is different from a replacement alternative to a particular experiment, such as a cell culture). Furthermore, how often do regulators pause to consider the validity of the tests they require for risk assessment – despite the fact that this should be their responsibility? The RSPCA believes these decisions should not be the exclusive province of the Home Office in assessing project licences or of scientific peer reviewers. A more flexible, (and therefore probably of necessity independent), element in the decision making process is essential.

In our view, scientific 'tradition' plays far too great a role in determining the approach to a scientific question and the research methods employed (including choice of species and techniques). It seems that the immediate response to any scientific problem is to create an animal model to try to answer it, because this is the way research in the life sciences has traditionally been done. The RSPCA believes that there is a need for far more innovative, creative, flexible and challenging thinking in research and toxicity testing in general with regard to the choice of method and the approach to asking and answering scientific questions. This necessitates a reconsideration of the way that science is taught and the way that students in the biomedical sciences are taught to think.

2.1.2 Some ethical questions regarding 'medical benefit'

It is argued that the public supports research on animals, including primates, when this is for medical benefit. However, there are many different 'publics' and no doubt many different definitions of medical benefit. A brief review of the uses of primates in research shows that they are often used to sort out problems that humans bring upon themselves, or to study non-life-threatening conditions, or to satisfy human aspirations and opportunism. Thus, they are described as 'ideal models' in anti-terrorism research programmes, studies of drug addiction, fertility, contraception and menopause research, in space research, and in the development of artificial intelligence systems including robotics.

This research is not just about curing serious diseases - there are economic, political, and competitive drivers. It is also about enabling people to indulge themselves and not accept the consequences. There is an entirely different ethical dimension to transporting primates across the world, confining them in laboratories, causing them pain, suffering and distress, and finally killing them, in order to study conditions that humans inflict upon themselves or for financial gain. The position of the public on this issue has not, to our knowledge been sought.

Public support for animal experiments means very little unless people are well informed on all the relevant issues. Surveys of public opinion offer very simplistic choices based on minimal information, and thus the public cannot properly weigh the harms to animals against the benefits to form a considered view. The benefits are always presented in very general terms and focus on curing obviously serious medical problems such as Parkinson's disease or Alzheimer's. The costs to animals are usually described in terms of involving only 'mild' procedures, carried out under high standards of husbandry and care. This is an extremely sanitised version of the true nature, level and duration of suffering (see section 2.4). There is little meaningful information within the public domain about what animals really experience.

2.2. The UK and global capacity to undertake primate research (terms of reference point 2)

Point 2 of the terms of reference refers to the intention: "*to assess the nature and implications of recent and prospective changes in the UK and global capacity to undertake primate research*". It is not clear what the study intends to 'assess' in this respect, e.g. whether it refers to the availability of primates, research infrastructure including facilities and expertise, or funding, or why this point has been included. These were the themes that ran throughout a workshop exploring the need for Rhesus monkeys in research, held in the USA in 2002[1]. The primary concern demonstrated at that workshop by primate users seemed to be whether they could access sufficient numbers of animals to supply an apparently increasing research demand, and at what

[1] Rhesus monkey demands in biomedical research. A workshop report prepared by the Research Resources Information Centre, Bethesda, MD 20814-3015. April 2002

financial cost. There was no mention of the serious animal welfare and ethical concerns, and the concept of alternatives seemed only to apply to developing models using alternative primate species rather than alternatives to animals per se. The RSPCA would be dismayed if a similar approach was repeated within this working group and would vigorously oppose any attempt to justify an increase in the availability or use of primates for research. The Society believes that, rather than worrying about whether primates will continue to be available, researchers should be more actively engaged in seeking ways to avoid the use of these animals.

It would have helped those asked to submit evidence if the purpose of 'point 2' had been explained. We will just outline our concerns on two issues, which we believe this point should cover – welfare aspects of the supply of primates, and training of staff caring for or using animals.

2.2.1 Supply

The RSPCA has many serious concerns about the acquisition of primates. These were described in the Society's report 'Counting the Cost', published in 2001[2]. Although the report was published four years ago, the concerns with regard to the continued use of wild caught animals as breeding stock, early weaning, barren, unenriched environments, long distance transport, and pre-export 'conditioning' still stand [3]. Indeed, 'conditioning' primates by housing them singly for long periods in tiny cages is one of the most inhumane practices the Society has identified. We fail to see how any researcher who believes they care for their animals' welfare can obtain them from sources that carry out such practices.

In our view, animals should be obtained from well resourced centres that do not capture animals from the wild, have good environmental enrichment programmes, wean at a minimum of 12 months (18 months for breeding animals), do not isolate and/or confine animals for conditioning purposes, and have sufficient well trained and experienced staff. Centres should also be as close to the place of use as possible to minimise transport stress.

2.2.2 Staff training

Reducing the suffering and improving the welfare of primates used in research requires staff to have a good understanding of the animals they care for, use, or require to be used, such that they can appreciate the impact of all aspects of the animals' lifetime experience. This requires special knowledge and practical skills and the RSPCA believes that current training is inadequate in this respect. A scientist can be an expert on primate 'models' of HIV, but have very little understanding of the *nature* of the primates he or she uses. The need for training and Continuous Professional Development (CPD) in a relevant scientific discipline may be taken for granted, but the need for training relating to the animals may not, even though good animal welfare is a prerequisite for good science. The accredited Home Office modular training is much too brief and in any case is only *an introduction* for prospective personal and project licence holders – a point made by the APC Education and Training Sub-Committee (which Dr Jennings chairs) in its current review of modular training. There are a very limited number of primate specific courses, but again these are short, and not everyone who needs them attends.

---

[2] Counting the cost: welfare implications of the acquisition and transport of non-human primates for use in research and testing. Mark J Prescott, RSPCA. (2001)

[3] Note that the APC Primate Sub-Committee is considering the acquisition of primates, including the recommendations in the RSPCA's report.

The importance of appropriate *primate-specific* training for *all* relevant categories of staff needs to be more widely accepted within the scientific community and time and resources must be allowed for this. Training courses need to be further developed and adequately resourced with sufficient availability for the different categories of staff that need them.

2.3 Alternatives to primates (terms of reference point 3)

The RSPCA believes that replacing and/or avoiding primate use should be accepted as a legitimate goal by government, industry and the scientific community and that a systematic and focussed strategy should be developed for achieving this. The Society is not alone in this respect. For example, the APC has the minimisation and eventual end of primate use and suffering as a stated goal [4], and the recent Nuffield Council report on The Ethics of Animal Experiments [5] states 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*". Although this is a statement about replacements generally, it clearly includes primates.

There are a number of technologies that have great potential for replacing experiments on primates and a very useful list of examples has been provided by The Dr Hadwen Trust in its submission to the Working Group. The RSPCA supports this approach and so will not repeat the same information in our submission to save space.

Additional resources need to be targeted at developing and validating (where necessary) humane alternatives, maintaining the focus on *replacing animals* rather than just developing and applying technologies. The RSPCA also stresses the importance of evaluating whether there are alternative ways of approaching research goals that will enable primate use to be avoided without needing to develop direct replacement alternatives.

2.4. Animal welfare issues and application of the 3Rs (terms of reference point 4)

Primates have a high level of cognitive development; they have intricate social relationships and behaviours; and they interact with their environment in a complex way and at many different levels. They engage in imaginative problem solving and exhibit a range of emotions. In short, they are very close to humans, a fact the users of primates argue make them ideal 'models' for research. However, this also makes them able to suffer like humans with respect to both physical *and* mental suffering (for example, they have been used to model depression and anxiety). Confining animals that would normally live in a very large home range in, at best, a small room and, at worst, a large metal box in which they can only take a few steps in any direction, must have a significant adverse effect on their welfare. Other aspects of the lifetime experience of the animals, particularly where they have no control of the environment, the situation or social grouping, also causes suffering [6]. The supply, transport, husbandry, identification, restraint, and euthanasia of primates thus all compound pain and distress associated with experimental procedures.

[4] The use of primates under the Animals (Scientific Procedures) Act 1986, analysis of current trends with particular reference to regulatory toxicology. Home Office. (2002)
[5] The ethics of research involving animals. Nuffield Council on Bioethics. (2005)
[6] See for example: The welfare of non-human primates used in research. Report of the Scientific Committee on Animal Health and Welfare, European Commission, Health and Consumer Protection Directorate-General. (2002)

It is therefore naive to believe that welfare can ever really be 'safeguarded' in the laboratory (as stated in the notes under 'scope'), because of the nature of the environment and what is done to the animals. Refinement can only mitigate the level of pain, suffering or distress the animals experience - it does not solve the problem. Nevertheless, refinement is critically important, and far more needs to be done in this respect – a general point made in reports by, amongst others, the Nuffield Council and the House of Lords[7]. This is important for science as well as welfare, since reducing stress in experimental animals leads to better science which in turn maximises the use of valuable resources including the animals lives. There is thus a very clear ethical (and scientific) imperative to define and implement refinements more actively and effectively.

There is already a great deal of information available about potential refinements to many of the situations and events that primates are likely to experience. However, this is not translated into practice at all establishments in the UK. RSPCA staff visit laboratories and discuss primate husbandry, care and use with the staff involved, and that it is clear many are still not aware of the full impact of their work on the animals, or of the potential for applying refinement and whose responsibility this is. Thus, we still see (for example) marmosets housed in tiered cages rather than allowing all animals to move above eye level, the use of grid floors which make foraging difficult, cages lacking an appropriate variety of enrichment, and insufficient training of animals to co-operate in procedures. Training can substantially reduce suffering, yet in a recent survey carried out jointly by the RSPCA and University of Edinburgh, it was clear that not all establishments were aware of the full potential for training their animals, or of how to do this despite extensive literature on the subject [8]. Note, the MRC has produced guidelines on primate husbandry and care [9] which are a significant improvement on the Home Office Code of Practice. All establishments should be required to implement these immediately if they do not already do so.

Under the scope of the study, it states that "*Practical measures to safeguard welfare and promote refinement within NHP research are being actively developed by several organisations, including the National Centre for the Replacement, Refinement and Reduction of Animals in Research"*. It is important to bear in mind that the NC3Rs can only cover a very small number of the many primate issues that need to be addressed, and appears to be mainly focussing on refinement in this respect. The Centre has a limited number of scientific staff to deal with such issues, has many other demands on its resources, and in any case at the time of writing has not defined its work programme and priorities. Responsibility for promoting refinement, or any of the 3Rs, cannot be devolved to any single body. It is the responsibility of all who create the demand for primate use, who fund it or carry it out.

****

Maggy Jennings BSc., PhD
Head of Research Animals Department, RSPCA
03.06.05

[7] Report of the Select Committee on Animals in Scientific Procedures, House of Lords. (2002)
[8] Prescott, M.J., and Buchanan-Smith, Training laboratory-housed non-human primates. Part 1: A survey of current practice in the UK (in preparation)
[9] Medical Research Council Ethics Guide: Best practice in the accommodation and care of non-human primates. (2004)