

Special Protection for Primates – the Need for Faster Progress

Maggy Jennings

RSPCA, Research Animals Department, Horsham, UK

Summary

The use of non-human primates in scientific research raises serious ethical and welfare concerns, which has resulted in legislation in some countries requiring special justification for the use of primate species. Furthermore, in the last ten years, there have been a number of authoritative reports urging tighter controls on primate use, higher standards of husbandry and care, and an end to the capture and use of wild animals. However, there appears to be great resistance to changing the status quo, and this paper will review whether progress has been made on any of these issues in the light of proposals for the revision of the EU Directive regulating the use of animals in experiments.

Keywords: *primates, legislation, Three Rs*

1 Introduction

The use of non-human primates in experiments is currently a hot topic of debate – something that could have been said at every World Congress since these began in 1993. However, it is particularly pertinent in Europe now, because Directive 86/609, which regulates animal experiments (European Community, 1986), is under revision and there is a good opportunity to incorporate provisions that would make a real difference to whether and how primates are used. Indeed, the notes in the introductory “Context Section” of the Commission’s draft proposal (European Commission, 2008a) state that: “*specific provisions have been incorporated to reduce the use of primates to a minimum*” and that “*there are ambitious requirements on the origins of animals and specific monitoring mechanisms to ensure the effectiveness of the proposed measures ultimately facilitating the move toward abolishing the use of non-human primates in scientific procedures.*”

This follows on from statements, reports and recommendations from authoritative national and international bodies, which highlight the need for further application of *all* 3Rs to primate use. The issue is firmly on the agenda, but the key question is whether anything is actually happening as a result.

There is progress in some scientific establishments in some countries, although mainly with the “R” of Refinement, but any progress in legislation seems extraordinarily slow and proposals for change encounter a high level of resistance. This paper therefore:

- reiterates why primates need special protection and what experimental use means for them – there is so much political wrangling this is sometimes forgotten;
- considers primate use in recent years and whether the trend in numbers is up or down;

- looks at some of the statements and recommendations made by European and national bodies that have an input into legislation to see whether these are taken into account in the proposed Directive; and
- makes a plea for more action on such recommendations now, not in the next one hundred years.

2 Why primates deserve special protection

Primates are highly intelligent, social animals. They occupy and interact with a large and diverse home range and have a complex range of behaviours and physical and emotional needs that are very difficult to satisfy in a laboratory environment. There is no question that they have the capacity to experience pain, and it should be assumed that procedures likely to cause pain and distress in humans are likely to have similar effects in other primates (e.g. Organisation of Economic Co-operation and Development, 2001; National Institutes of Health, 2002). It is also generally accepted that they can experience both negative emotions (fear, anxiety, boredom, frustration and, in some species, grief) and positive emotions (interest, pleasure, happiness, excitement) (see Jennings and Prescott, 2009).

The impact of a laboratory environment

It seems something of an anomaly that researchers who study primates in the wild emphasise their amazing capabilities, which are brought to television screens around the world for people to marvel at, and admire. Yet in the laboratory, these animals are confined in small cages, subjected to invasive procedures and treated in a reductionist way as research “tools”.

Compare and contrast the natural and laboratory environments for macaques and marmosets, for example. The natural



habitat of long-tailed (cynomolgous) macaques is forest, commonly near water, a complex three dimensional environment. Their home range is around 2 km², reaching from ground level to tree-top height. They live in social groups of 10 to 50 animals, with sometimes as many as 100, and are very active – walking, leaping, climbing, foraging and swimming. They have extensive sensory and communication abilities with a perceptual world similar to humans.

Contrast this with a laboratory environment. The Guidelines for Accommodation and Care of experimental animals in the recently revised *Annex II* of EU Directive 86/609 require a minimum cage area of 2 m² with a height of 1.8 m. The standards are intended to encourage pair housing but some places still keep animals singly. In any case, this only allows animals to take a few steps in each direction and can never offer much complexity; it is barren and boring. In effect, animals that have evolved to live in a forest are consigned to a small metal box.

Marmosets also live in family groups of 2 to 15 animals in complex forest habitats with a range of .006 to 0.06 km². They, too, are very active animals with a diverse sensory world. In the laboratory they may fare slightly better, being kept in pairs or family groups, but they are still very confined with the standards for cage size being a mere 0.5 m² in area and 1.5 m in height.

Cumulative harms

Given the nature of primates and the difficulty of providing for their needs, it is generally considered that the cumulative harms for these animals are greater than for other animals. As well as restricted housing and the effects of experimental procedures, there are significant welfare issues with respect to capture and use of wild animals, early weaning, transport, pre-transport “conditioning” in tiny cages for long periods in some supplying centres, and handling and restraint. In fact the animals’ whole lifetime experience is seriously compromised.

Public and political concern

There is a high level of public and political concern about the use of primates – people have a special affinity with these animals as fellow primates. This was illustrated in the European Commission survey of public opinion in 2008 when over 93% of respondents believed it was important to improve the current level of welfare/protection for primates in research and testing (European Commission, 2006).

3 Trends in primate use

Given the level of concern about primate use it might be expected that this would have had an effect on the numbers used, but this is not so. Figures for primate use over the last ten years do not show a decrease. For example, in the UK, numbers fluctuate around 3500 per year. Figures for Europe show an increase in

primate use from 7284 in 1999 to 10,443 in 2007¹, as do figures in the USA where numbers have risen from around 55,000 in 1999 to nearly 70,000 in 2007². Furthermore, some scientists are talking about a likely increase in the need for primate use for “biological” pharmaceutical products and research into diseases of ageing. Even the use of chimpanzees has not been ruled out, and countries in Asia are known to be increasing their primate research capacity.

4 Legislation and relevant reports and statements

Legislation is a major driver of change as are, or should be, recommendations in reports commissioned or developed by legislative or regulatory bodies. There are many of these covering issues such as: the capture and use of wild primates; their accommodation and care; and the necessity and justification for using them. Some of the key recommendations made over the last fifteen years or so by formal European and national bodies are summarised below with a consideration of whether and how these are being taken forward in the revision of Directive 86/609.

Capture and use of wild primates for breeding or experiments

It is accepted that capture of animals from the wild and their use in experiments is a major stressor for primates (e.g. Johnson et al., 1973; Laudenslager et al., 1999; Suleman et al., 2004). The issue was mentioned in the report of the 1993 Berlin Workshop on the accommodation of laboratory animals. The workshop was organised by the German Federal Ministry of Food, Agriculture and Forestry, in conjunction with the Federal Health Office supported by Directorate-General XI of the European Commission (O'Donoghue, 1994). The aim was “to review critically” the standards of accommodation in the European Convention and Directive “in the light of knowledge gained since they were formulated”. The report recommended that the use of wild-caught primates should be phased out completely within five years.

Then, in 1997, the Council of Europe issued a Declaration of Intent: “to require precise information on the origin and the provenance of the animals (primates) with the objective of limiting the use of animals to those which are purpose-bred”; and “to encourage initiatives and measures to end the use of wild-caught primates” (Council of Europe, 1997). The Declaration was signed by sixteen Member States and twelve stakeholder organisations, including Eurogroup for Animal Welfare, Federation of European Laboratory Animals Science Associations (FELASA), Federation of European Laboratory Animal Breeders Associations (FELABA), European Federation of Pharmaceutical Industries Associations (EFPIA) and European Biomedical Research Association (EBRA). The following year the issue of capture of wild primates was mentioned in the recitals to the Council of the European Union’s decision to approve

¹ Figures for the EU are available from the tri-annually produced official reports: http://ec.europa.eu/environment/chemicals/lab_animals/reports_en.htm

² Figures for the US are available from the Annual Reports of Enforcement (Animal Welfare Act) produced by the USDA (see Appendix 5 of 2007 report): http://www.aphis.usda.gov/animal_welfare/publications_and_reports.shtml

the European Convention on animal experiments. There then followed a number of authoritative national and international reports, which re-emphasised concerns over the capture of wild animals and argued the need to use only purpose-bred primates and move to the use of F2³ animals (e.g. Animal Procedures Committee, 2002; Scientific Committee on Animal Health and Welfare, 2002).

How does this translate to the revision of the Directive? The draft proposal to revise 86/609 stated in its Article 10.1 that there should be a “move to exclusive use of F2 macaques, seven years after transposition of the Directive”. Seven years is a long time, but this at least threw down a definite marker. However, despite the level of concern over primate capture, the European Parliament’s report on the draft modified the text and introduced the need for a feasibility study for moving to exclusive use of F2 animals. Subsequent discussions allowed up to five years for such a study to be carried out. If this procedure is agreed, and assuming the Directive is accepted in 2010 with an immediate start to the feasibility study, then in 2015, eighteen years after the 1997 Declaration of Intent, there *may* be a decision about whether a move to F2 can be achieved – at some stage! This is surely an inexcusable amount of time to deal with an issue that all stakeholders have agreed is a serious problem.

Accommodation and care

Turning to husbandry standards, again there is a long history of reports and comments on the inadequacy of housing and care for primates in the laboratory environment. The Berlin Workshop report clearly stated that the “existing [1986] recommendations for primate housing in the Council of Europe Convention are inadequate”. It went on to state that: “the sizes of cages are too small to meet the behavioural needs of the animals; they provide neither adequate space for exercise nor room for environmental enrichment”. The report made recommendations to the Council of Europe and the European Commission for improvement.

Five years later, in 1998, the Council of Europe began the process of revising Appendix A to the Council of Europe Convention (Council of Europe, 2005 on the use of animals for scientific purposes in which standards of accommodation and care for laboratory animals are set out. (The minimum cage size for one or two 15–25 kg macaque at the time was 1.5 m² x 1.25 m). The process was an extended one with revised standards developed through working groups of experts from the stakeholder groups of animal welfare, academia, industry and regulation. It was finally concluded in 2006. The revised standards for cage sizes have since been translated into the Annex to Directive 86/609, but with a date of 2017 allowed for their adoption. Thus, *twenty-four years* after it was agreed that existing standards were inadequate, primates may have 0.5 m² extra space! However, at the time of writing, the European Parliament’s report on the draft Directive allows exemptions and reduces the status of the standards to guidelines instead of mandatory requirements.

Fortunately, some establishments already use the new standards and improve on them further, but this is by no means universal, and many macaques are still kept in small inadequate housing.

Necessity and justification for primate use

In some countries, such as the UK, concern over primate use is reflected in legislation with “additional justification” required before such animals can be used, together with exclusions on the use of wild-caught animals and Great Apes. A number of national and European reports have urged more critical scrutiny of the necessity and justification for primate use including the Scientific Committee on Animal Health and Welfare Report (SCAHAW, 2002), the UK Animal Procedures Committee (APC) report on primate use in regulatory toxicology (Animal Procedures Committee, 2006) and most recently the Scientific Committee on Health and Environmental Risks report on primate use (SCHER, 2009).

Particularly relevant in the context of the proposed EU Directive is a 2007 European Parliamentary Declaration, which called for a timetable for replacing all use of primates (European Parliament, 2007). The European Commission responded to this with reference to the Directive, which it said could “*incorporate strong incentives together with a specific review clause which would provide a mechanism to move towards the ultimate goal of phasing out primate use*” (European Commission, 2008b). The Commission went on to say that it was convinced this goal could only be achieved with a “*vision, close co-operation and combined effort of all concerned*”. Animal protection organisations had said something very similar in a “Resolution” on primate use passed four years earlier at the World Congress in Berlin. The Resolution urged “*governments, regulators, industry, scientists and research funders worldwide to accept the need to end primate use as a legitimate goal; to make achieving this a high priority; and to work together to facilitate this*”.

Has any of this been carried through into the revision of the Directive? As quoted earlier in this paper, there are strong statements in the introductory “Context” section of the Commission Proposal, but these are not carried through into the articles. This makes no progress at all for primates and does not reflect the spirit of the “Background” and “Recitals” text. However, it is positive to see a ban on the use of Great Apes, although extremely disappointing that it was deemed necessary to insert a “safeguard clause” to allow their use in an “emergency”. Quite what emergency would warrant subjecting chimpanzees to confinement in a metal box is beyond imagining, even if the practical difficulties of acquiring, housing and using such animals within a rapid response scenario could be overcome.

There were restrictions on the use of other species of primate; use had to be undertaken “*with a view to the avoidance, prevention, diagnosis or treatment of life-threatening or debilitating clinical conditions*”. Despite the fact that spokespersons in the research community argue in public that all primate research

³ F2: Second generation animals whose parents were captive-bred.



is undertaken for serious medical purposes – and would therefore be allowed to continue even with the proposed restriction – there was a great deal of lobbying against this requirement. As a result, the parliamentary report removed the restriction on use but added in a “two year review” of primate use to examine the impact of developments in technological, scientific and animal welfare knowledge and set targets for implementation of validated replacement methods. What form this should take was not specified.

5 What is now needed

Looking at the timelines on the way these issues have been dealt with, the idea of progress is a misnomer. What is needed is fewer words and more action. It is true that some people, at some establishments, in some countries, have put a lot of effort into refinement and improving housing and care. However, much more immediate action is necessary if this is to be more universal and if the many good recommendations that have been published in reports and the scientific literature are to be translated into real achievements in Reduction and Replacement (or avoidance) of primate use as well. In Europe, the Directive can help if the requirements for an authorisation process and ethical review remain, but specific restrictions on primate use are also necessary.

Legislation, of course, will not work alone, and there are some useful recommendations that need translating into practice. The SCHER Report, for example, provides a useful starting point with its recommendations for:

- regular meetings to stimulate scientific discussions and exchange of information;
- development of databases and collaborative user networks covering data sharing, tissue sharing, exchange of knowledge and information;
- global networks to exchange information on the 3Rs, including providing clear and consistent guidance on the criteria for use of primates; and
- further negotiations between the EU, USA and Japan on harmonisation of regulatory test requirements

A UK committee comprising the major research funders in 2006 also made useful recommendations including: to undertake a systematic review of research funded in the last ten years; and to regularly collate and disseminate information about evolving research technology (Anon, 2006). Two years later there is no information in the public domain as to whether this is being taken forward, but it could be done through:

- focussed reviews of the validity and need for primate use in individual research and testing fields carried out by teams of open-minded multidisciplinary experts
- a co-ordinated, well-funded international effort to support a transition from animal-based toxicology to a mechanism-based paradigm; and
- a fundamental shift in attitude away from the defensive “why primates are essential” to a constructive exploration of “how the research goals could be achieved without them”.

Finally, the essential point missing from most reports is a properly structured implementation plan for the recommendations they contain, with clearly defined responsibilities and some challenging timelines. This is what is desperately needed to achieve progress for these animals sooner rather than later, i.e. now, not in 100 years time.

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Correspondence to

Dr Maggy Jennings BSc PhD
RSPCA, Research Animals Department,
Wilberforce Way, Southwater,
Horsham, West Sussex,
RH13 9RS, UK
e-mail: mjennings@rspca.org.uk