Parliamentary Office of Science and Technology

postnote

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ANIMAL PROCEDURES

Use of animals in scientific research is regulated under the Animals (Scientific Procedures) Act 1986. In March 2001, the House of Lords convened an ad hoc Select Committee to investigate the workings of this Act and to examine issues relating to the use of animals in research. This note was prepared at the request of this Committee; it provides background briefing on the terms of the 1986 Act, and recent trends in animal use.

Animals (Scientific Procedures) Act 1986

What is an animal?

In its original form, the Act defined 'protected animals' as all living[1] vertebrates except humans. It has since been was amended to include an additional (invertebrate) species: *Octopus vulgaris*. The Act applies to all of these species only after they have reached certain specified stages of development.

What is a scientific procedure?

A 'regulated procedure' is defined in the Act as any experimental or other scientific procedure applied to a protected animal which may cause pain, suffering, distress or lasting harm. This definition does **not** include procedures involved in standard veterinary, agricultural or animal husbandry practices, but **does** include the:

- Breeding of animals with genetic defects;
- Use of animals to produce certain blood preparations such as antisera;
- Use of animals to maintain/produce tumours or parasites;
- Administration (for scientific purposes) of drugs to dull perception (anaesthetics, analgesics, tranquilisers).

Licences

Two types of licence are required under the Act:

- Project licences - all procedures must be carried out as part of a licensed programme of research;
- Personal licences - all people carrying out procedures on animals must also hold a personal licence.

Project licences

The Act requires the potential costs (in terms of the adverse effects on the animals) of proposed research to be weighed against the likely benefits (e.g. to humans, other animals or the environment). Home Office Inspectors (HOIs, see Box below) are responsible for making such judgements. They agree an overall severity band for the project based on the amount and duration of suffering caused, number of animals used, and whether anaesthetics are used or other action is taken to reduce suffering. Severity bands for the 3,481 project licences in force in the UK in 1999 are given in the Table overleaf. Assessing potential benefits is difficult because scientific research is, by its very nature, unpredictable. Overall, there are no hard and fast rules for weighing benefits against costs although the HOI ensures that alternatives to animals are considered and that research complies with the principles embodied in the 3Rs:

- Replacement - use of alternatives to animals (Page 4);
- Reduction - using the minimum number of animals;
- Refinement - use of procedures that minimise the amount of pain and suffering.

The Home Office Inspectorate (HOI)

The 1986 Act established the Home Office Animals (Scientific Procedures) Inspectorate, which operates the licensing system on the Home Secretary's behalf and advises Ministers on animal policy. All Inspectors hold medical or veterinary qualifications. Their duties include:

- processing applications for new licences/certificates;
- amending the terms of existing licences/certificates;
- revoking licences where appropriate;
- inspecting designating premises to check compliance with the terms of certificates and licences.

In 1999 (the most recent year for which figures are available) 21 Inspectors operated from five regional offices: Cambridge, Dundee, London, Shrewsbury and Swindon. They made some 2,174 inspections during 1999 (on 31 December 1999 there were 296 designated premises and 3481 project licences in the UK). All told, action was completed on some 28 infringements of the Act in 1999.

Severity bands for project licences in force in 1999

Severity band	Number	%
Mild	1406	40.4%
Moderate	1861	53.5%
Substantial	66	1.9%
Unclassified[1]	148	4.2%
Total	**3481**	**100%**

1. *Projects in this category inflict no pain or suffering on the animals – they are decerebrate or the entire procedure is carried out under anaesthetic.*

Personal licences

These are designed to ensure that any person conducting animal procedures is suitable and competent to do so. Applicants must be 18 years or older, and must have completed an accredited training course. They must provide full details of education, qualifications and relevant experience; those applying for a licence for the first time must also have endorsement from a suitably qualified sponsor. Personal licences are reviewed every 5 years and revoked if the researcher is no longer active. In 1999, there were around 13,700 active personal licences in the UK; some 1,791 new licences were granted and 1,862 revoked.

Designation of premises

In addition to personal and project licences, the Act requires procedures to be conducted in specially designated premises[2]. In order to receive a certificate of designation, premises must meet certain standards of animal housing and care; designated premises are subject to regular visits from HOIs (see Box Page 1). Establishments that breed certain types of animal for laboratory use, and those that obtain or supply laboratory animals must also have certificates of designation. In 1999, there were 296 designated premises in the UK; all are required to nominate someone to take responsibility for the day to day care of animals, and a vet to advise on animal health and welfare.

Trends in animal procedures

As outlined in the Box opposite, the HOI collects information on a wide range of different aspects of animal use in scientific procedures. The last year for which such data is available is 1999. This section presents some of the main recent trends.

Overall number of procedures

Post-war trends in the number of animal procedures are shown in the Figure opposite. Between 1946 and the mid-1970s, the number of experiments involving animals rose steadily from around 1.5 million to well over 5.5 million. Since this peak, the numbers have declined, albeit with a 'blip' after 1987, due to a switch from experiments to procedures following the 1986 Act. Some 2.66 million procedures were conducted in 1999 involving around 2.57 million animals (some animals are used in more than one procedure).

Species

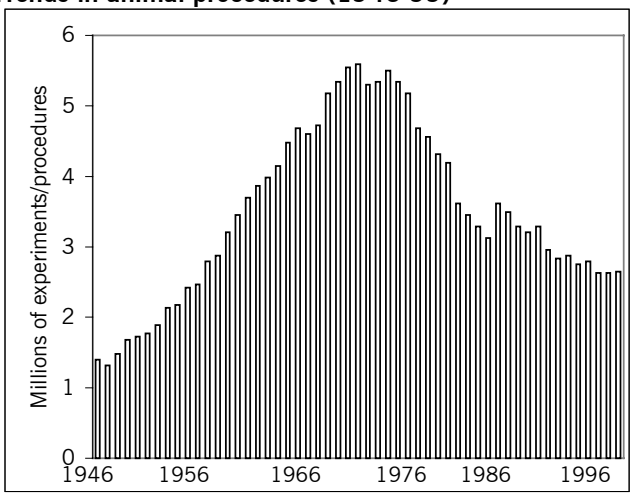
Rodents – particularly mice and rats – account for the large majority (83% in 1999) of all animal procedures (see Figure, Page 3). The 'other mammals' shown in the Figure are primarily guinea pigs, rabbits, ungulates (sheep, pigs and cattle) or rodents other than mice and rats. Relatively few procedures conducted during 1999 involved cats (1,623) dogs (8,185) or primates (4,003).

Information collected by the HOI

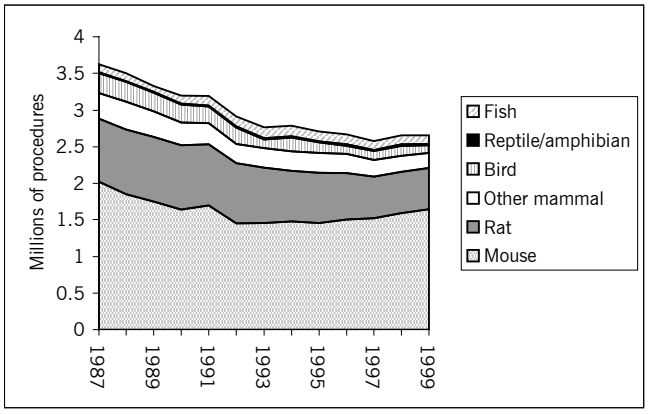
Each year, project licence holders have to fill in and return a form detailing information about the procedures started under the project in that year. Questions asked relate to:

- Species of animal(s) used in procedure(s).
- Is it on the CITES endangered species list?
- Stage of development of the animal. Only adult and free living (i.e. newborns and older) animals are counted in the statistics; they do not include procedures involving larval/embryonic or foetal stage animals.
- Genetic status – animals are classified into one of three categories: genetically normal, harmful mutants (animals with a harmful genetic defect) and genetically modified (e.g. transgenic) animals.
- Source – this applies to animals listed in Schedule 2 of the Act (mouse, rat, guinea pig, hamster, gerbil, rabbit, dog, cat, ferret, primate, quail and genetically modified pigs and sheep). Licence holders must specify where these animals were acquired from (e.g. in-house, from a designated UK breeding/supply establishment, from a non-designated UK source, from another country within the EU, or from a country outside of the EU).
- Anaesthesia/NMBA – was anaesthetic used, at what stage in the procedure, did the animal recover, was a neuromuscular blocking agent (NMBA) used?
- Primary purpose of the procedure – the Act allows procedures for: fundamental biological research; applied studies in human medicine/dentistry or in veterinary medicine; protection of man, animals or the environment (toxicological or similar tests); education; training; forensic inquiries; direct diagnosis; breeding.
- Body system – what was the primary target body system (respiratory, cardiovascular, nervous, etc.)?
- Toxicological or similar tests – what was the purpose (e.g. nature of the substance tested and why) and type (e.g. chronic or acute toxicity, carcinogenicity) of test and was it required by law?
- Fundamental and applied studies (non-toxicological) – what was the primary field of research (anatomy, physiology, biochemistry, etc.); was the procedure for the production of biological materials, for breeding or another purpose; were techniques of particular interest (involving the brain, stress, trauma, etc.) used?
- Total number of procedures and animals (were animals used in more than one procedure?).

Trends in animal procedures (1946-99)



Trends in species used in animal procedures (1987-99)



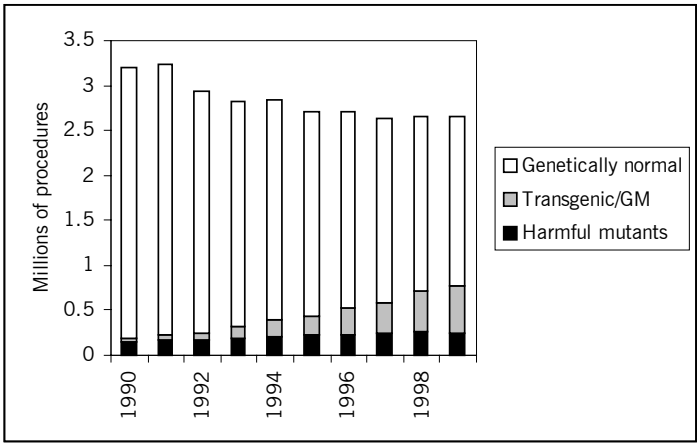
Genetic status

A particular trend during the 1990s has been the emergence of procedures involving animals that have been genetically altered. These include:

- Animals that have been bred to possess harmful genetic defects (mutants).
- Transgenic animals – animals that express a gene (or genes) inserted from another individual of the same species, or from a different species altogether. Transgenic animals were recognised as a separate category in Home Office statistics in 1990.
- Genetically modified (GM) animals. More varied techniques for genetically altering animals have now been developed. For instance as well as inserting novel genes, it is now also possible to 'knock out' specific genes. 'GM animals' is thus a wider definition, embracing transgenic as well as animals genetically altered by other methods; it replaced the transgenic category in Home Office statistics in 1995.

Recent trends in procedures involving animals of different genetic status are shown in the Figure below. There has been a steady decline in the number of procedures using genetically normal animals, from just over 3 million in 1990 to slightly under 1.9 million in 1999. The same period has seen an overall rise in the use of animals with harmful mutations (from ~143,000 to ~251,000) although the number of procedures in this category dropped between 1998 and 1999. More consistent has been the rise in procedures using transgenic/GM animals, which has increased tenfold since 1990 (from just under 50,000 to over 500,000). These trends mean that GM animal procedures accounted for nearly one in five of all procedures in 1999.

Trends in procedures by genetic status (1990-99)



Mice account for the overwhelming majority of procedures involving harmful mutants (88%) and GM animals ((98%). One reason for this is that the mouse genome has been highly studied and the similarities between it and the human genome are well documented. A detailed discussion of the reasons behind the rise in use of GM animals[3] is beyond the scope of this briefing although much of it is accounted for by:

- Using GM animals to create better models of human disease, especially those caused by faults in one gene.
- Studies designed to increase understanding of gene function use GM mice to 'knock out' (or over-express) a specific gene to see what happens.
- Toxicity testing using GM animals. Commercial strains of mice are available that allow the easy detection of mutations caused by chemicals, or that are more susceptible to developing mutations in cancer-related genes. Use of such strains is controversial; while they may reduce the overall number of animals needed, there are animal welfare implications of using mice 'designed' to develop cancer.

It is likely that the recent upward trends in GM animal use will continue in fundamental research and for commercial purposes. For instance GM animals may be:

- used for making therapeutic proteins secreted in milk (several companies have already done this);
- used as a source of tissue for xenotransplants (although there are safety concerns over this area);
- developed for agriculture (although there are concerns over animal welfare and public acceptance).

Purpose of animal procedures

Home Office statistics have two main categories of purpose for animal procedures: toxicological and similar safety testing (often conducted for regulatory purposes), which accounted for over 20% of procedures in 1999; and other fundamental or applied studies (~80%).

Toxicological and similar tests

In all, toxicological and similar (e.g. efficacy tests, testing substances to see whether they cause mutations or cancer) tests accounted for just over 540,000 procedures in 1999. The vast majority (86%) of these were required by safety regulations (UK, EU or other international regulations). Most (65%) involved the testing of pharmaceuticals, for safety, efficacy, quality control or other purposes. In previous years, certain types of tests – or the testing of certain types of products – have been the focus of debate. These include:

- LD50 (lethal dose 50%) tests – these tests are carried out to establish the safety/toxicity of chemicals and drugs. They raise obvious animal welfare concerns because they involve establishing the dose level that kills 50% of the animals dosed. In October 1999, the Home Office announced that licences would no longer be granted to perform such tests if a suitable alternative were available. BUAV[4] and other groups

argue that suitable alternatives are available and that no further licences should be granted for such tests. The problem is that some foreign regulatory regimes still specify LD50 tests. According to the APC, the Home Office estimate that such procedures account for up to 2,000 animals per year.

- Cosmetic tests – animal procedures involving cosmetics were a big issue in the early 1990s (~4,400 such procedures were conducted in 1990). In November 1997, the Government announced that licences would no longer be granted for testing finished cosmetic products; this was extended in 1998 to include testing of ingredients primarily intended for cosmetics. Thus, in 1999, no animal procedures involved testing cosmetics or their main ingredients.
- Testing of tobacco products – in November 1997, the Government also announced that it would not allow animals to be used for the development and testing of tobacco products. No animals were thus used for such purposes in 1999.

Other fundamental or applied studies

These accounted for some 2.1 million procedures in 1999. Pharmaceutical research and development was the largest single field of research, accounting for some 482,000 procedures, closely followed by immunology (318,000) and cancer research (267,000). Anaesthetics were used to minimise pain and suffering in around 40% of procedures conducted in this category; the majority (60%) of procedures were too minor for anaesthetic use to be considered appropriate.

Weighing costs and benefits

As noted previously, the 1986 Act requires decisions on whether to grant project licences to weigh the costs to the animals involved against the potential benefits arising from the proposed research. A 1997[5] review of the Act by the Animal Procedures Committee (APC)[6] included a number of comments on the weighing of costs and benefits. Many of the comments considered this approach to have contributed to animal welfare, although the review also highlighted concerns over the way such assessments operate in practice.

As a result of these concerns, the APC recently (February 2001) conducted a consultation exercise on cost/benefit assessment seeking views from interested parties in three main areas. First, is the scientific validity of animal experiments. Those opposed to animal experiments sometimes argue that the physical and physiological differences between animals and humans mean that animals are not valid models for studying humans. The APC sought views on the criteria that can be used to assess the validity of animal experiments, and whether the current cost/benefit assessment adequately addresses concerns over validity.

Second, is the identification and weighing of costs and benefits. In particular, the Committee sought views on:

- Experiments involving some types of procedure (e.g. tests of alcohol, tobacco and cosmetics) and some types of species (e.g. great apes) are ruled out by the Home Office (HO). Are there additional groups of procedures that should be viewed as unacceptable?
- Are there some types of benefit that might not justify the use of animals?
- Are all relevant costs and benefits identified by current HO practice?
- Should assessment of costs be restricted solely to consideration of the procedures? Or should they include a wider consideration of costs associated with capture, confinement, transport, etc.?
- Are there specific costs associate with GM animals?

Finally, the APC consultation sought views on developing good practice for such assessments. The Committee was keen to hear from people in other fields – human clinical trials, environmental risk assessment, etc. – who make decisions based on assessments of costs and benefits.

Alternatives to animal use

The Act requires alternatives to animals to be used where possible. Groups such as FRAME and the RSPCA[7] promote the concept of alternatives to the use of live animals in research and testing. In the short-term they see reduction and refinement as the main ways forward. Reducing animal use can be achieved by better experimental design, multiple use of animals, improved access to databases, and harmonising regulations. Refining procedures to minimise pain and suffering may involve using of anaesthetics/analgesics and non-lethal endpoints. In the longer term, such groups hope that research on alternatives may eliminate the need for live animal experiments altogether. Research areas include:

- Use of lower order species (insects, bacteria or plants).
- Development of in vitro techniques using cultures of animal or human cells, organs or tissues. Examples include the development of artificial skin for toxicity testing, and the use of embryonic stem cells to test chemicals for effects on embryos.
- Use of computer models to simulate interactions between different body systems.
- Increased use of human volunteer studies.

Endnotes

1 The Act defines an animal as living until 'the permanent cessation of circulation or complete destruction of its brain'.
2 Except where the project licence allows procedures to be conducted elsewhere (e.g. field work at a specified place and time).
3 The use of GM animals is a subject that is currently being considered by a Royal Society Working Group, which is expected to publish a report in May 2001. It is also the subject of a forthcoming POSTnote.
4 British Union for the Abolition of Vivisection
5 See the APC 1997 Annual Report (http://www.apc.gov.uk/)
6 The APC is an independent committee set up by the 1986 Act with wide powers to advise the Home Secretary on policy and practical matters relating to the Act.
7 Fund for the Replacement of Animals in Medical Experiments and the Royal Society for the Prevention of Cruelty to Animals

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